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Sheep and Goats in the Epidemiology of Q Fever in Northern California:

The investigations of the Australian workers indicate that in Australia Q fever is a natural infection of cattle (and bandicoots), and is transmitted among them by ticks. The human disease is thought to represent aberrant infections, which are outside the basic cycle, and result from inhalation of dried infected tick feces or tissues present on the hides of cattle; a history of tick-bite in human cases has been uncommon.

The two outbreaks of Q fever which occurred in this country at Amarillo, Texas, and Chicago involved in both instances persons connected with meatpacking plants. The source of infection was considered to be infected cattle at Amarillo and infected calves or sheep at Chicago. In the Los Angeles area, cases have not been limited to groups occupationally associated with cattle, but have occurred as well in persons using raw cow's milk or living in areas adjacent to dairies or livestock yards. In Northern California, on the other hand, human cases appear to be at least as frequently associated with contact with goats and sheep as with cattle. The results of serologic studies indicate that infection with Coxiella burnetii is much more prevalent in sheep and goats (37.9 and 43.6 percent respectively) epidemiologically linked with human infections than in cattle (2.6 percent) associated with human cases.

Information accumulated from serologic surveys of the general domestic livestock population, including sheep, goats, cattle, horses, swine, and poultry, gives no evidence that species other than the first 3 are infected. These surveys further show that the extent to which infection is present in sheep and cattle in the general population not only is very small, but is essentially similar in both species (too few goats were available for analysis). Moreover, the findings obtained in the endemic area were not significantly different from those in the control area.

The marked difference between the extent of infection encountered among sheep associated with human cases and that found in the general sheep population, even in the endemic area, suggests that the causal rickettsia has been introduced into the sheep population only relatively recently; otherwise, were this a disease of long standing, it would seem that the infection should be seeded more or less uniformly throughout the sheep in the area, and the remarkable differences found here would not exist. The proportion of sheep associated with human cases and possessing antibodies is high; the proportion of sheep possessing antibodies in the general livestock population is low. It seems reasonable to believe that this difference is not fortuitous but arises either from some causal relationship between the human and the sheep disease, or perhaps is referable to a common factor operating independently on each species. The same situation probably exists concerning goats and man, although data from the general goat population are too few to permit a similar comparison. In cattle epidemiologically associated with human cases, the prevalence of infection, as judged by serologic

methods, was found to be similar to that in cattle from the general animal population. This suggests that the role of cattle in the epidemiology of the human disease in Northern California is secondary to that of sheep and goats. The excretion of the rickettsiae in the milk of sheep and goats (and cattle) is an important epidemiologic finding because such excretion provides a mode of exit for the organism not dependent upon arthropods. The presence of the rickettsia in milk constitutes an obvious potential source of infection, but what the method of transmission might be is essentially unknown.

In the authors' experience, a history of tick-bite in human cases of the disease has been exceedingly rare (one case), and livestock examined have been found surprisingly free of arthropod infestation. Caminopetros reports that sheep and goats develop bronchopneumonia following nasal instillation of the rickettsia. Dissemination of the infection among animals and its spread to man by means of infected respiratory tract secretions thus appears possible. Because the rickettsiae are excreted in the milk, ingestion of milk or its products also may afford a possible means of infection. Finally, contamination of the environment by infected body secretions would permit wide dispersal of the causal agent through dust, and might explain the occurrence of infections in individuals who have had no contact with livestock. Air-borne spread of the infection through dust contaminated with the rickettsia appears to be the most likely explanation of such outbreaks as those which occurred among Allied troops in northern Italy in 1944-1945 and among United States troops returning to this country from southern Italy in early 1948, and in which exhaustive investigations gave no evidence that any other modes of transmission were involved. Robbins and his associates state that in the northern Italian outbreaks the association of patients with dust was quite striking; many of them had used hay for bedding, and it is of interest that others were billeted in dusty quarters which also housed cattle and sheep, or had sheltered goats. The outbreak affecting troops returning from Italy developed among 5 squadrons which had been stationed at the Grottaglie Air Base in southern Italy. It is stated that the infection was clearly acquired at this air base. The opportunities for generation of dust at any air field are obvious, and although Grottaglie base was not considered to be any dustier than other air fields in the same region, it is again of interest to note that sheep and goats were pastured nearby. More recently, Wegmann has reported on an outbreak of Q fever, affecting 19 persons, in which the infection was believed to be caused by inhalation of infected dust from straw in packing cases received from the United States.

Because C. burneti is resistant to a number of physical and chemical agents which are lethal for most micro-organisms, its ability to survive for indefinite periods of time in desiccated body secretions seems probable, and its dissemination by dust aerosols would therefore appear to be a plausible mode of transmission. In this connection, C. burneti has been recovered from the dust from sheep pens on a ranch where animals were known to be excreting the organism in the milk. (Am. J. Trop. Med., July '49, E. H. Lennette et al.)

Effects of Adrenocorticotrophic Hormone on Neuro-Muscular Function in Patients with Myasthenia Gravis: The adrenocorticotrophic hormone (ACTH) of the pituitary gland has been administered to patients with myasthenia gravis mainly on the basis of the following observations and inferences: (1) The immediate cause of the symptoms of myasthenia gravis is a decrease of acetylcholine synthesis. (2) Administration of the adrenocorticotrophic hormone increases acetylcholine synthesis *in vivo*. (3) Increase of the lymphatic tissue, round-cell infiltration of various organs, mainly striated muscle, and hyper-functioning thymus have been found in patients with myasthenia gravis. Tissue fractionation studies have shown that one of the sources of the substances that inhibit acetylcholine synthesis is the thymus. Administration of the adrenocorticotrophic hormone induces reduction in the mass of the thymus and the lymphatic tissue. (4) Removal of the pituitary gland in rats induces changes in the electromyogram that closely resemble the abnormalities noted in patients with myasthenia gravis. (5) The pituitary gland of several patients who died of myasthenia gravis showed accumulation of an eosinophilic colloid material suggesting altered function of the gland.

Five patients with myasthenia gravis were women aged 24 (H.L.), 29 (J.R.), 31 (M.Y.), 37 (A.S.), and 45 (R.G.) years who had had myasthenia gravis for 4, 17, 10, 13, and 9 years, respectively. During the 3 years before this special study was begun the patients experienced minor transient fluctuations but no long lasting or significant changes in their clinical states. They received a total of 300, 45, 180, 112, and 150 mg., respectively, of neostigmine bromide a day, distributed over the waking hours, taken in from 3 to 6 hourly intervals. H. L. received also 75 mg. of ephedrine sulfate, 3 Gm. of potassium chloride, and 0.39 Gm. of guanidine hydrochloride a day; R. G. also received 25 mg. of ephedrine sulfate and 3 Gm. of potassium chloride a day. The patients had had, in different degree of severity, anorexia, general weakness, ptosis of the eyelids, weakness and easy fatigability of the muscles of the palate, tongue, face, deglutition, arms, and legs. Various tests were performed on these patients for one week. Thereafter they were given intramuscularly 20 mg. of ACTH every 6 hours for 5 days. Tests were performed during the administration of the hormone, for 4 days thereafter, and at biweekly intervals for another 12 weeks.

During the 5 days of administration of ACTH all patients experienced a gradually increasing disability lasting until the second day after the completion of the injections. Thereafter, the patients exhibited increased well being, they began to reduce the daily intake of neostigmine bromide spontaneously (H.L. from 300 mg. to 45 mg., M.Y. from 150 mg. to 15 mg., A.S. from 112 mg. to 15 mg., R.G. from 180 mg. to 90 mg., and J.R. from 45 mg. to 15 mg.) and omitted the other medications. A partial remission of the symptoms occurred in all instances manifesting itself in marked decrease of muscle weakness, the easy fatigability, and the anorexia. The ptosis of the eyelids, the weakness and easy fatigability of the muscles of palate, tongue, face, deglutition, arms,

and legs became less evident. There was a disappearance of the abnormalities noted in the electromyogram and an increase to normal in the ability of the serum to support acetylcholine synthesis. However, the remission was incomplete; the muscle groups most severely involved in each patient showed only a partial recovery, as is to be expected after a muscle dysfunction of several years' duration. Though not clearly definable, it is probable that there is some dwindling of the improvement in muscle function with the lapse of time. This incomplete remission persisted from the completion of administration of the hormone to the writing of this report, a period of approximately 3 months. (Proc. Soc. Exper. Biol. and Med., July '49, C. Torda and H. G. Wolff)

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The Relationship of Gastric Acidity to Gastric and Extragastric Neoplasms: The association of achlorhydria and hypochlorhydria with gastric carcinoma is a fact that has been noted by many observers and has been stressed in the diagnosis of gastric cancer. It was the purpose in this study to investigate the relationship between gastric acidity and extragastric malignancies.

All patients over the age of 50 years registering at the outpatient clinics of the Minnesota University Hospitals for the first time were subjected to a gastric analysis employing 3 successive doses of 0.5 mg. of histamine, given hypodermically, as a stimulant to gastric secretion. Topfer's reagent was used to test for free hydrochloric acid, and quantitative estimations were made using $\frac{N}{10}$ NaOH and Topfer's reagent as the indicator. In a number of instances the patients for one reason or another were not given the 3 conventional doses of histamine, but they did receive one or 2 injections of histamine, and these patients were included in the statistical data. Patients not receiving histamine were excluded from the study. Patients who had no free hydrochloric acid after histamine stimulation were considered to be achlorhydric. Those who had free hydrochloric acid following histamine stimulation were further subdivided into (a) hypochlorhydria group - maximum free hydrochloric acid not exceeding 29° , (b) normal acidity group - free acid ranging between 30° and 49° , and (c) hyperchlorhydria group - free acid exceeding 50° . The diagnosis of the tumors was based on microscopic examination of a section taken from a biopsy specimen or from the tumor itself after excision.

Included in the study were 1,315 patients over the age of 50 years. Two hundred forty-four patients had extragastric malignant lesions and the incidence of achlorhydria and hypochlorhydria in this group was 32.8 percent and 24.6 percent, respectively. The incidence of achlorhydria and hypochlorhydria in 93 patients with benign extragastric tumors was 30 percent and 28 percent, respectively. Achlorhydria and hypochlorhydria occurred in 36 percent and 23 percent, respectively, of 906 patients with non-neoplastic disease. Of 57 patients

with gastric carcinoma, 85 percent were achlorhydric and an additional 5 percent were hypochlorhydric. Thirteen patients with gastric polyps all had achlorhydria, although of 2 patients with leiomyoma of the stomach one had achlorhydria and the other hyperchlorhydria. Achlorhydria and hypochlorhydria occur significantly more frequently in patients with cancer of the stomach than in patients with extragastric malignant tumors. The incidence of achlorhydria and hypochlorhydria of the latter group is practically the same as for the individuals with non-neoplastic disease of the same age group. (Surgery, July '49, S. Niazi et al.)

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Treatment in Nausea and Vomiting of Pregnancy with Dramamine:

Nausea occurs in approximately 50 percent of pregnancies, and in about 25 percent vomiting ensues. The severity of symptoms varies in individual patients. The cause of these symptoms has never been definitely established. Coincident with the study of the control of motion sickness with dramamine, it was decided to investigate the effect of the drug on nausea and vomiting in pregnancy.

Forty-three women who had complained of these symptoms for from 4 to 6 weeks had been given a number of remedies but experienced no relief. Each was given 100 mg. of dramamine, 3 times daily. This dose was reduced to 50 mg. 3 times daily for 7 patients because of minor side-effects, drowsiness, and vague subjective muscle tremors. Unknown to 10 patients, the drug was discontinued and a placebo of lactose, identical in appearance, was substituted. Thirty-one patients (72.1 percent) of the 43 were completely relieved of their symptoms 3 hours after administration of dramamine. Ten patients whose symptoms were controlled by the drug relapsed when a placebo was substituted, but regained their normal health after dramamine was again administered. Twelve patients (27.8 percent) of the 43 obtained no relief from the drug.

Although the number of patients treated with dramamine is small, the results are so encouraging that the Allergy Clinic and the Obstetrical Clinic of the Johns Hopkins Hospital and University are making an extensive comparative study. (Science, 26 Aug. '49, P. E. Carliner et al.)

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Chloramphenicol (Chloromycetin) and Aureomycin - Therapeutic Results:

Burkholder first isolated from soil the streptomyces from which chloramphenicol is derived and demonstrated its antibiotic activity. In the research laboratories of Parke, Davis and Company, Ehrlich and his associates further extended studies of the antibiotic activity and prepared the compound in crystalline form

to which was given the name chloromycetin (Parke, Davis & Company's trade name). The compound is neutral containing both nitrogen and nonionic chlorine. Its solubility in water at 25° C. is about 2.5 mg. per cc. It withstands boiling for 5 hours and in aqueous solutions over the pH range of from 2 to 9 is unaffected by standing at room temperature for more than 24 hours. Chloramphenicol is well absorbed from the gastro-intestinal tract. Serum levels after oral administration have been found comparable to those obtained by parenteral administration. There are no reports up to the present time of toxic manifestations resulting from the oral administration of chloramphenicol. The prolonged intramuscular administration in dogs resulted in a moderately severe anemia without significant changes in the white blood cells and without disturbance in hepatic or renal functions.

The initial studies of the antibiotic spectrum of chloramphenicol in vitro and in vivo in animals indicated a wide range of usefulness, particularly in rickettsial and Gram-negative infections. These investigations demonstrate outstanding effectiveness in rickettsial and psittacosis infection of chick embryos and mice. Among the Gram-negative organisms showing a considerable degree of sensitivity to this antibiotic are the brucellae, members of the salmonella group and coliform bacteria. It is interesting to point out that up to the present time chloramphenicol has not failed to exert great beneficial effect in those clinical diseases whose etiologic organisms have been found sensitive to the agent when tested in the laboratory.

Aureomycin, first isolated by Duggar, is a yellow crystalline antibiotic obtained from the mold recently characterized Streptomyces aureofaciens. It is freely soluble in distilled water at a concentration of 2 percent and produces a golden yellow solution having a pH of 4.5. The antibiotic is most stable at pH 2 and an unbuffered aureomycin hydrochloride solution at pH 2.9 has been maintained at cold room temperature \pm 4° C. for 23 days with no measurable loss of activity. Aureomycin has low toxicity and when administered in intravenous doses of 50 mg. per Kg. in dogs, cats, rabbits, guinea pigs and mice no symptoms are observed. Multiple intravenous doses in dogs produce irritation of the perivascular tissues at the site of injection, and subcutaneous and intramuscular injections are likewise irritating. After oral administration, aureomycin appears in the urine in one hour and is excreted up to 12 hours. Therapeutically effective concentrations exist in the cerebrospinal fluid within 6 hours after an intravenous dose. A turbidometric assay has been described for determining the concentration of aureomycin in body fluids. This test has not proved of great value clinically because of the relative instability of this compound.

The in vitro and in vivo range of activity of aureomycin very closely approximates that of chloramphenicol. Similarly, its greatest influence is on the rickettsiae and on the viral agents of the psittacosis-lymphogranuloma group. When tested in vitro against brucellae, effective inhibition is demonstrated and

most salmonellae are inhibited by aureomycin in the range of from 1 to 25 micrograms per ml. Both Proteus vulgaris and Pseudomonas aeruginosa are relatively resistant to aureomycin but unlike chloramphenicol most strains of Gram-positive cocci, pneumococci and hemolytic streptococci are actively inhibited by this antibiotic. Aureomycin appears to be bacteriostatic in its effect. Bacteria do not readily become resistant to aureomycin in vitro, nor is there evidence of cross resistance with other antibiotics.

Typhoid Fever. In all but one of the 21 patients here reported the diagnosis was confirmed by a blood culture positive for Salmonella typhosa prior to the initiation of specific therapy. Patients were selected for treatment who were in an active phase of disease and in most instances within the first 2 weeks of illness. The mean day of illness that treatment was begun in this series of cases was the twelfth.

Chloramphenicol was administered orally in the form of 0.25 Gm. tablets and capsules furnished by the Research Division of Parke, Davis and Company. The initial dose was large, gauged on the basis of approximately 50 mg. per Kg. body weight. After the initial dose the drug was given in 0.25 Gm. doses at varied intervals but usually every 2 or 3 hours. In certain of the early cases the antibiotic was given first on a 2-hour schedule which was changed to the longer interval when improvement was noted. The program of treatment adopted included continuation of the drug for 5 days after the temperature had reached normal levels. In certain instances the author and co-workers were forced to discontinue treatment earlier because of exhausted supplies. Vomiting of the drug on initial administration occurred rarely but in no instance necessitated discontinuance of therapy. The average total dosage per patient was 22.7 Gm. given over a period of 9.1 days. There was little subjective improvement within the first 48 hours of treatment. By the third day, however, there was obvious abatement of headache, cough, and delirium and it was apparent on the fourth day that the patient was in convalescence showing interest in his surroundings, with increased strength and appetite. Rose spots noted in approximately half of the patients were observed to disappear by the end of the second treatment day. Irrespective of the height of the preceding fever, the age of the patient, or the day of illness treatment was begun, chloramphenicol therapy was followed in all instances by fall of temperature to normal levels within 4.5 days after the initial dose. The average duration of fever after initiation of therapy was considerably less, approximately 3.5 days. Normal temperature was defined as oral temperature remaining under 99° F. and rectal temperature under 100° F. In all instances reduced toxicity paralleled or preceded the return of temperature to normal. In 20 patients blood cultures taken prior to initiation of specific therapy were positive for S. typhosa. In 18 of the 21 cases blood cultures were taken daily for from 3 to 5 days following the initiation of treatment. In 4 patients blood cultures were found positive, 2 during the first 24-hour period and 2 during the second 24-hour period. The subsequent cultures remained sterile.

except in the case of patients who suffered a relapse. Stool cultures were obtained at frequent intervals, and no patient was discharged without 3 consecutive negative stool cultures. Positive cultures were obtained in 6 patients at least one time while chloramphenicol was being administered and in 4 patients after the antibiotic had been stopped. The stools of all 4 patients with relapses contained S. typhosa. Urine cultures before the beginning of specific therapy, during therapy, and in convalescence were consistently negative.

The blood level for chloramphenicol was followed in 17 patients throughout the course of treatment. The blood concentration of the drug during the first 24 hours of therapy was from 30 to 80 gamma per ml. and during the subsequent period of from 3 to 5 days averaged 20 gamma per ml. Workers at the Research Division of Parke, Davis and Company had previously shown that S. typhosa is inhibited by concentrations of chloramphenicol of approximately one-quarter gamma per ml. when the 50-percent end point technic is applied to fluid culture. Utilizing practically identical methods, the author and co-workers found the sensitivity of the infecting organisms in this series to range from 0.25 to 0.26 gamma per ml. In no instance when additional tests were made on organisms causing a relapse or after termination of chloramphenicol therapy was in vitro resistance of the organism observed. The evidence indicated that the clinical manifestations of typhoid fever were definitely suppressed by use of the drug and moreover complete disappearance of the S. typhosa from the blood stream and from the stool was evident in 13 of the 21 cases. However, that such complete sterilization was not always attained is evidenced by the data concerning the remaining 8 cases. In 4 instances follow-up stool cultures were found positive on at least one or 2 occasions. In 4 cases positive blood cultures recurred and in all of these the reinvasion of the blood stream was evidenced by clinical relapses. There were 4 relapses in 21 cases, the recurrences beginning on the ninth, twelfth, thirteenth, and thirteenth days, respectively, following discontinuance of treatment. In 3 instances the organisms found during the relapse were tested and found not to have lost their sensitivity to chloramphenicol. This was confirmed in 3 cases by the treatment for the relapse with chloramphenicol with resultant prompt clinical cure. Certain of the usual complications of typhoid fever may occur either during treatment or after treatment has been discontinued. In 2 instances intestinal hemorrhage was observed after the patient had become afebrile but was still under treatment. In another case perforation occurred under the same circumstances; in this patient with all the clinical characteristics of perforation, the peritonitis was overcome without surgical treatment, apparently as a result of continued chloramphenicol treatment supplemented by penicillin and streptomycin. Another instance of what may have been a late complication was that of an elderly man who after discharge from the hospital as cured of typhoid returned in 10 days with low-grade fever and died suddenly with a massive pulmonary embolus (confirmed by autopsy) which was suspected though not proved to have originated from a late typhoid phlebitis.

Aureomycin was used in 4 cases of typhoid fever, using an initial dose of from 1 to 2 Gm. followed by a schedule providing from 0.50 to 0.70 Gm. every

4 hours in adults and 0.25 Gm. every 4 hours in children. An antipyretic effect occurred in 2 patients but the typhoid toxic state continued and no improvement was apparent. Two of these 4 patients survived; the febrile course in one was 26 days and in the other 50 days. Two patients succumbed; one on the 22nd day of illness after a total of 13.8 Gm. of aureomycin and the other on the 19th day after receiving 13.0 Gm. of aureomycin for 3 days. Ross *et al.* report in detail the findings in 3 patients with typhoid treated with aureomycin. They conclude that aureomycin did not produce any perceptible reduction in the duration of illness in 2 patients but suggest that the acute phase in a third case may have been favorably influenced. Finland *et al.* detailing the results of aureomycin in 5 patients with typhoid conclude that the therapeutic effects were equivocal. Both of these groups of workers report the clearing of the blood and stool of *S. typhosa* after several days of aureomycin treatment. Chloramphenicol is clearly the drug of choice in clinical typhoid. The optimum course of treatment remains to be determined.

Brucellosis. Eight patients manifesting evidence of active infection with brucellosis have been treated with chloramphenicol. Treatment was initiated when the clinical evidence available suggested brucellosis and when laboratory findings were confirmatory. The dosage regimen adopted for the study was empirical and based, in general, upon prior experience in scrub typhus and typhoid fever. The initial dose based on approximately 50 mg. per Kg. body weight was adhered to and the subsequent schedule was 0.25 Gm. given every 3 hours until at least 5 days of normal temperature ensued. In all instances the antibiotic was tolerated well orally and no clinical evidences of toxic effects were observed. The average total dosage per patient was 19.7 grams given over a period of 8.1 days. The mean duration of fever prior to treatment in the 8 treated patients was 30.7 days. Two of these patients were more seriously ill than the others. Within 36 hours after the start of specific treatment they were resting more comfortably, spent a more restful night for the first time since the onset of illness, and diaphoresis was greatly reduced. In the remaining 6 patients there seemed to be immediate improvement of the body and joint pain, added strength, and a decidedly improved taste for food. In the 8 patients the mean duration of fever after beginning chloramphenicol treatment was 2.4 days. The spleen, found enlarged in 6 patients, was observed to become nonpalpable during the course of antibiotic treatment or shortly thereafter. Of these 8 patients, 4 showed a positive blood culture for *Brucella abortus* and 2 for *Brucella suis* prior to giving chloramphenicol. All of the post-treatment blood cultures remained sterile. The sensitivity of the infecting organisms isolated from the 5 patients ranged from 0.78 to 2.4 gamma per ml. (These concentrations compare favorably with those reported by Smith *et al.* who have previously demonstrated inhibition of brucellae by chloramphenicol in the following concentrations: *B. abortus* 2.0 gamma per ml., *B. suis* and *B. melitensis* 0.5 gamma per ml.) This small group of patients has shown no complication attributable to brucellosis. A period of 8 months has elapsed since 6 of these patients

were treated. A recurrence of symptoms has not been observed, the patients are ambulatory and afebrile, and blood cultures taken on the 3-month follow-up examination remain sterile. During this same period the agglutination titers have uniformly decreased.

Aureomycin was used in the treatment of 5 patients. Except in one instance when repeated laboratory tests could not be performed, the criteria outlined for the above group were adhered to. An initial oral dose of one Gm. of aureomycin was given followed by a dose of 0.5 Gm. every 4 hours for 3 days and then 0.5 Gm. every 6 hours for an additional period of from 5 to 11 days. In one instance because of exhausted supplies, a short course of 8 days was given. The average total dose per patient was 21.99 Gm. given over a period of 11.6 days. No clinical evidences of toxicity were observed other than nausea and occasional vomiting and diarrhea. The mean duration of fever prior to treatment in the 5 patients was 39 days. The response to treatment in these patients closely parallels the pattern observed with chloramphenicol. Within 48 hours after instituting treatment clinical improvement was noted, the patients uniformly felt stronger, and there was a noticeable increase in appetite and vigor; aching of the muscles and joints lessened, and the nocturnal diaphoresis was considerably lessened. In all 5 of these patients the P.M. temperature for at least one week prior to the institution of treatment was 102° F. or above. The mean in the 5 patients for duration of fever after beginning aureomycin was 3.8 days. The fever in no instance recurred once a permanent normal level was attained. In 2 patients the spleen was observed to become nonpalpable during the course of treatment. Blood cultures in 2 of the 5 patients were found positive for B. abortus prior to treatment. Cultures taken several times during the course of treatment were sterile, and in 3 patients cultures taken one month following discharge were negative. In 4 patients a rising titer for B. abortus agglutinins was demonstrated and in the fifth a titer of 1/1280 was found after repeated tests. The sensitivity of the 2 organisms isolated from 2 patients was 0.45 and 0.23 gamma per ml. respectively. Complications were not encountered. Two patients are now 4 and 5 months convalescent, and 3 patients are now about 2 months past treatment and all remain well.

Bryer *et al.* reported B. abortus and B. suis sensitive to aureomycin in the concentration of 0.75 gamma per ml. They reported a favorable response to this antibiotic in a patient with chronic B. suis infection. The patient became afebrile in 3 days, and blood cultures became sterile 48 hours after treatment was begun. Ross *et al.* similarly describe a favorable response to aureomycin in a 48-year-old farmer with an acute exacerbation of chronic brucellosis and a positive blood culture. The temperature reached normal in 3 days, and he was symptomatically normal within 5 days. Later blood cultures were sterile. Spink *et al.* give detailed accounts of a larger series of patients treated in Mexico. In 24 patients with Brucella melitensis infection aureomycin produced prompt reduction of toxemia and return of temperature to normal in 72 hours. Three relapses were later observed.

Tularemia. Data published earlier by the author and co-workers include the comparative results with chloramphenicol and streptomycin in experimental tularemic mouse infections. These data show that aureomycin has apparently a more effective protective action against Pasturella tularense in mice than streptomycin. Under the same conditions the protective action of chloramphenicol appears to be less than that of streptomycin or aureomycin.

The schedule of treatment with aureomycin in 3 seriously ill patients conformed closely to that employed in undulant fever. An initial dose of one gram was given with subsequent doses of 0.5 Gm. every 4 hours. The ulceroglandular form of the disease complicated by a bilateral pneumonia was present in one patient, and 2 patients were of typhoidal type, both with pneumonia. The response to treatment in all was immediately favorable; within 24 hours the degree of toxemia was greatly reduced and the signs of weakness, cough and anorexia rapidly improved. The average duration of illness prior to treatment was 9.6 days, and the average duration of fever after beginning aureomycin was 2.5 days. Laboratory confirmation of a specific diagnosis for tularemia was obtained in each case. P. tularense was obtained from the sputum of 2 patients through mouse inoculation, and from the other patient when pus from the primary ulcer and bubo was inoculated subcutaneously into mice. Agglutinins in high titer ranging from 1/1280 to 1/5120 were demonstrated in all patients. The development of pleural effusion was the lone complication in one instance. The further course in the patient was uneventful. The author and co-workers have not treated any patients with tularemia using chloramphenicol.

Results with the use of streptomycin in human tularemia are well known to be highly specific. Berson *et al.* reported that in 56 patients clinical improvement was observed within 48 hours after instituting therapy with streptomycin, and the mean time for attaining normal temperature was 7 days. In 67 patients reported upon by Keefer *et al.* there were 63 recoveries and 4 fatalities. In 55 the results were regarded as striking and immediate. Two relapses occurred in this series. In patients with tularemia treated with streptomycin by others the temperature returned to normal in periods ranging from 2 to 6 days. P. tularense has been found to disappear from the sputum and pleural fluid soon after administration of streptomycin. *

The fatality rate in tularemia complicated by pneumonia has been estimated to be as high as 30 percent. Each of the 3 patients here reported had pneumonia. The patient with the ulceroglandular type of tularemia would undoubtedly have died without chemotherapeutic help. His rapid recovery is attributed to aureomycin. The ease of administration of aureomycin and its apparent freedom from toxic complications justifies a further clinical comparison with streptomycin in tularemia.

Rickettsial Infections. The efficacy of chloramphenicol as a chemotherapeutic agent in experimental rickettsial infections was first demonstrated

by Smadel and Jackson. Results obtained with the use of this antibiotic in embryonated eggs and mice experimentally infected with the agents of scrub typhus, epidemic typhus, murine typhus, Rocky Mountain spotted fever and rickettsial pox indicated high specificity of action. An excellent chemotherapeutic effect was obtained in mice when administration of drug was delayed for 10 days after infection. Smith *et al.* concluded from chick embryo testing that chloramphenicol gram per gram was more effective against Rickettsia prowazeki (epidemic typhus) than streptomycin, para-aminobenzoic acid or methylene blue. The antirickettsial action of aureomycin was demonstrated in experimental infections of embryonated eggs, mice, and guinea pigs against the agents of murine typhus, epidemic typhus, Rocky Mountain spotted fever, Q fever, rickettsial pox and scrub typhus by Wong and Cox. No *in vitro* activity was demonstrated. Regardless of the length of time fever had been apparent in guinea pigs infected with Rocky Mountain spotted fever, epidemic typhus and Q fever, the animals were in most instances rendered afebrile within from 48 to 72 hours by a single daily subcutaneous injection of from 5 to 6 mg. of aureomycin per kilo for from 3 to 5 days. It has been shown that injection of a massive dose of infectious material into guinea pigs if followed by aureomycin treatment before symptoms appear, results in no signs of illness in the animal, but antibodies in measurable degree are induced and the animals become immune to subsequent challenge. If guinea pigs receive small doses of infectious material and then are treated with aureomycin before symptoms appear, neither fever nor other signs of illness develop, but antibodies do not always appear and the animals are often susceptible on rechallenge.

Scrub typhus. The mean day for beginning treatment with chloramphenicol in 25 patients with scrub typhus after the onset of illness was 6.2 and the mean duration of fever after beginning specific therapy was 31 hours. A reduction of the toxic state was observed to antedate the return of temperature to normal in all instances. Rickettsiemia was demonstrated in 20 of the 25 patients by animal inoculation and a positive Weil-Felix reaction was demonstrated in 24. All patients received an initial dose of approximately 50 mg. per kilo and were subsequently given from 0.2 to 0.3 Gm. of drug by mouth at periods of from 2 to 4 hours for a varied length of time. The duration of treatment was eventually shortened to cover a 24-hour period. Patients received about 6 Gm. of chloramphenicol during this short period of therapy, and the uniform prompt clinical response to this short course of therapy further attests to the highly specific effect which chloramphenicol exerts in this rickettsial disease. Relapses in the naturally occurring disease were not observed. This series of patients has now been extended to a total of 69. Similar results, using aureomycin, have been obtained by the U. S. Army scrub typhus team.

Epidemic typhus. Smadel and his associates administered crystalline chloramphenicol orally to 5 patients with epidemic typhus fever in Mexico. The clinical diagnosis in all was confirmed by the demonstration of rising titers for

agglutinins against *Proteus OX 19*, and complement-fixing antibodies. Two of the adult patients in this small series appear to have been very favorably benefited by chloramphenicol. The response in one patient appeared equivocal, perhaps because of the small doses of antibiotic employed. Two children with mild epidemic typhus were apparently benefited by this therapy. Payne in a series of 22 patients with typhus treated with chloramphenicol reports prompt reduction of toxemia in critically ill patients. There are no reports of patients treated with aureomycin.

Murine typhus. Ley and his collaborators treated 3 patients with murine typhus with chloramphenicol. Laboratory confirmation of the clinical diagnosis in each instance was by demonstration of increasing titers of complement-fixing antibodies and rickettsial agglutinins utilizing murine typhus antigens. *Proteus OX 19* agglutinins were also present. Mean values for duration of illness prior to beginning treatment was 8.7 days and duration of fever after beginning specific therapy was 53 hours. Dosage schedules are comparable to those used in scrub typhus. Three patients do not permit statements of any statistical significance pertaining to therapeutic effectiveness. Nevertheless, the course of illness in one case coincides in general with the pattern of response observed in scrub typhus and other rickettsial infections.

A patient with murine typhus was diagnosed and treated with aureomycin by Dr. William Schulze of Greenville, South Carolina. The patient, a 45-year-old woman, experienced continuous fever and a body rash was observed on about the eighth day of illness. Aureomycin was started on the tenth day of illness with 0.5 Gm. orally every 4 hours for 2 days and 0.5 Gm. every 6 hours for a total of 5.5 days of therapy. The temperature, plateau-like at 103° to 104° F. at the time of beginning treatment, descended by rapid lysis and became normal 36 hours later. The symptoms rapidly subsided and convalescence was uneventful. Complement-fixing antibodies for murine typhus were 1/128 on the twelfth day of illness and 1/256 on the eighteenth day. The Weil-Felix titer was positive at 1/80. In a discussion of the aureomycin treatment of Rocky Mountain spotted fever, Hill stated that he treated 8 patients with murine typhus with this antibiotic and reported the period of prostration reduced by about from 5 to 6 days, as compared with cases on supportive therapy alone. The temperature returned to near normal in 3 days.

Based upon the meager clinical evidence available it appears that both chloramphenicol and aureomycin exert specific benefit in murine typhus. The clinical response in this benign rickettsial disease is similar to that observed in other members of the group. It is not possible to distinguish between the efficacy of either agent in the small series of cases reported.

Rocky Mountain spotted fever. A study by Pincoffs *et al.* describes the results obtained in the treatment of Rocky Mountain spotted fever with chloramphenicol. Fifteen authenticated cases comprise this series. A history of

exposure to ticks was present in all patients, fever had been continuous from the day of onset, a rash was uniformly present, and secondary clinical features commonly observed in this disease such as headache, mental dullness, delirium and tarsal conjunctivitis were commonly observed. The diagnosis was confirmed in each instance by the presence of one or more of the following: (1) isolation of rickettsiae in guinea pigs, (2) agglutinating titers for Proteus OX 19 of 1/160 or higher, and (3) complement-fixing antibodies in rising titer. Clinical improvement shown by the abatement of headache, mental dullness, etc., was definite within 24 hours of therapy. By the third day the patients were plainly convalescent. The average duration of fever after initiation of specific therapy was 2.2 days. Evidences of any toxic effect of the drug were not observed.

Fortunately reports on comparable series of patients with Rocky Mountain spotted fever treated with aureomycin are available. Thirteen patients fulfilling the clinical and laboratory criteria outlined above were treated by Ross *et al.* in various clinics in Maryland and the District of Columbia. An initial loading dose of aureomycin was employed, administered on the basis of from 2 to 5 mg. per kilo at hourly and 2-hourly intervals during the active stages, changing to 4-hour intervals when the temperature reached normal. The average amount of aureomycin administered per patient was 9.5 Gm. given for a mean period of 6 days. The authors state that the optimum dose has not been determined. The rash disappeared within from 3 to 5 days after the initiation of drug therapy in patients treated within the first 4 days of disease. The temperature subsided rapidly within an average of 2.3 days. Striking clinical improvement was likewise observed. Toxic manifestations other than nausea and vomiting were not encountered. Cooke describes an additional patient treated on the fourth day of illness whose temperature reached normal 48 hours after institution of aureomycin treatment. Harrell's results in 3 additional patients are similar.

The demonstrated efficacy of PABA (para-aminobenzoic acid) in Rocky Mountain spotted fever and other rickettsial infections has been shown. Toxicity is reduced and the temperature reaches normal after beginning this therapy in periods ranging from 6 days in one series of 17 patients to 3 days in a similar series. On the other hand, PABA must be administered in very large doses, the blood electrolyte status must be closely evaluated, and after prolonged administration the agent may show evidences of being hepatotoxic. Chloramphenicol and aureomycin apparently obviate these undesirable traits of PABA with the possible exception of aureomycin which causes slight nausea. Each of these antibiotics, however, exerts a more rapidly favorable influence on the course of Rocky Mountain spotted fever than does PABA. With the evidence available one cannot distinguish between the relative efficacy of either antibiotic at the present time.

Q Fever. Published accounts relative to the treatment in human cases of Q fever are limited to aureomycin. Lennette and his co-workers treated 19 patients in California. The duration of fever was selected as the best objective

criterion for the evaluation of the therapeutic effect of the drug. Individuals 26 years old or older were chosen for treatment because this group had been shown to have a long and stormy course. In 10 patients treated during the acute phase fever continued for an average of 3.0 days after beginning therapy. Symptomatic improvement was noted within 48 hours. Two relapses occurred attributed by the authors to a suppressive rather than a killing effect of the antibiotic on the infecting agent.

Viral-Like Infections. Both aureomycin and chloramphenicol show marked therapeutic effect in mice which have been infected intraperitoneally or intracerebrally with the agents of psittacosis and lymphogranuloma venereum. Results obtained in embryonated eggs infected with these agents are essentially identical. It is to be emphasized that neither chloramphenicol nor aureomycin has shown therapeutic activity against other experimental virus infections.

Lymphogranuloma venereum. Wright *et al.* report 25 patients with lymphogranuloma venereum treated with aureomycin. Eight of these patients with buboes showed decided reduction in size of the node at the end of 4 days' treatment and elementary bodies were observed to disappear from the glands within one week of treatment. Three patients with proctitis showed prompt and decided improvement, whereas 14 patients with rectal stricture appeared to show only amelioration of the rectal pain, discharge and bleeding. The dosage of aureomycin was small, ranging from 10 to 40 mg. per day, administered intramuscularly.

The author and co-workers have administered chloramphenicol to one patient with lymphogranuloma venereum of the glandular type without proctitis. The bubo decreased appreciably in size within 5 days of treatment, and elementary bodies were observed to disappear from the enlarged gland as determined by animal inoculation and by direct examination of prepared smears. The diagnosis in the patient was confirmed by isolation of the elementary bodies in mouse brain and by complement-fixation tests.

Psittacosis. One patient with ornithosis made a dramatic response to aureomycin. The patient received aureomycin on the seventh day of illness, and the response to treatment was immediate. The disease was characterized principally by a bilateral pneumonitis and severe headache. Proof of diagnosis was by demonstration of complement-fixing antibodies in the titer of 1/128. One week prior to onset of illness the patient had trapped 80 pigeons in the rafters of his barn.

Primary atypical pneumonia. The viral-like agent causing this disease has been successfully transmitted to normal human subjects. A similar pneumonitis has been observed in diseases with specific etiology, such as influenza,

psittacosis, ornithosis, tularemia, and the rickettsial diseases, particularly Q fever. Thus, in a study of atypical pneumonia a specific diagnosis must be searched for. There are now 3 independent series of patients treated with aureomycin in whom the diagnostic possibilities mentioned above have been considered. Schoenbach and Bryer, Finland *et al.*, and Kneeland *et al.* report successful treatment in primary atypical pneumonia with this antibiotic. It was universally observed by these 3 groups of observers that the fever and symptoms began to improve promptly after beginning specific treatment and the temperature was normal usually within 48 hours.

The results of the author and co-workers in the treatment of atypical pneumonia of nonspecific etiology are confined to 3 patients. Two patients treated with aureomycin made a recovery very similar to that observed in the reported cases. One patient with the typical roentgen evidence of this condition responded equally favorably after the use of chloramphenicol. It is of interest to point out that as a result of the screening routine which the author and co-workers have adopted for the diagnosis of pneumonitis, they were successful in finding the specific etiology of ornithosis in one instance and of tularemia in another. (Ann. Int. Med., July '49, T. E. Woodward)

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Chloramphenicol (Chloromycetin) in the Chemoprophylaxis of Scrub Typhus (Tsutsugamushi Disease) - Epidemiological Observations: The prevention of scrub typhus is an important civilian and military problem throughout much of the Asiatic-Pacific area. Although procedures of immunization have not proven effective in the field, measures directed against the mite vector have succeeded in greatly reducing the infection rate among exposed military populations. A third method of prevention, chemoprophylaxis, was subjected to extensive field trials by the United States Army Scrub Typhus Unit working at the Institute for Medical Research, Kuala Lumpur, during the spring and summer of 1948. The results of these studies are reported elsewhere. In conducting these field trials it was necessary to locate and study certain focal areas of hyperendemicity.

Several hyperendemic areas of scrub typhus in the vicinity of Kuala Lumpur, Malaya, were investigated. All areas were covered by secondary or scrub vegetation generally consisting of a wide variety of shrubs, grasses, vines and weeds, and were infested with a heavy population of native, mite-infested rats. In agreement with the observations made by others a number of years ago in Malaya, and more recently in New Guinea, Assam and North Burma, Trombicula akamushi or Trombicula deliensis, or both, were abundant in the areas where human cases of scrub typhus were contracted. Although sharp seasonal changes are absent in Malaya, periods of relative drought do occur. During one of these, the number of Trombicula decreased markedly in an area

where they had previously been numerous and had constituted the majority of mites carried by wild rodents. Concurrently with the increase in aridity of the area, an absolute and relative increase in numbers of nonvector mites was noted on the captured rats. Even in small portions of fields where the vegetation was essentially similar throughout, marked differences were noted in the numbers of Trombicula observed on volunteers, and on experimental rats exposed within a few feet of each other. It seems likely that unfed larvae do not wander far but become highly active when stimulated.

The majority of Trombicula found on rats exposed for 40 hours were engorged indicating very rapid feeding. Attached mites observed on human beings at 3:30 p.m., which presumably had been acquired 5 or 6 hours before, were generally still present at 7:30 p.m. but usually not the following morning. Trombicula larvae were most active in the morning when the dew was evaporating. They were least evident during the heat of the day. An appreciable proportion of the Trombicula larvae collected in the areas under investigation from wild rats, exposed white rats, and quail were infected with Rickettsia tsutsugamushi.

In the first test ever carried out in which volunteers were purposely subjected to the chance of infection with R. tsutsugamushi by exposure in fields known to be hyperendemic foci of scrub typhus, 29 of the 46 persons contracted the disease. Exposure of 29 other individuals in these same areas at a somewhat later date, when Trombicula were relatively scarce, resulted in infection of only 8 of the volunteers. (Am. J. Hyg., July '49, C. B. Philip et al.)

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Chloramphenicol (Chloromycetin) in the Chemoprophylaxis of Scrub Typhus (Tsutsugamushi Disease): Chloramphenicol has been shown to be a highly effective therapeutic agent in experimental rickettsial infections; furthermore, laboratory studies suggested that this drug might be a useful prophylactic drug against scrub typhus in man. Accordingly, when the results of studies on patients with tsutsugamushi disease indicated that this once dread infection could be reduced to a nonfatal illness in which the fever terminated, on the average, in 30 hours after chloramphenicol treatment was begun, it seemed appropriate to proceed to test the chemoprophylactic value of this drug in men exposed to scrub typhus under natural conditions. Epidemiological studies had shown that there were several well delimited areas where scrub typhus was hyperendemic in the vicinity of Kuala Lumpur. Field tests were undertaken in which volunteers were exposed in selected areas and given chloramphenicol as a prophylactic measure or a placebo of calcium lactate.

The 22 volunteers who received chloramphenicol in the first test were each given 1.0 Gm. daily in divided doses throughout the 9-day period of exposure and for 13 days thereafter. Each man received 0.25 gram orally at

8:00 a.m., 0.50 gram at 12:00 noon and 0.25 gram at 4:00 p.m. The second field trial was undertaken to determine whether administration of drug at weekly intervals would provide a suppressive effect on Rickettsia tsutsugamushi which was comparable to that obtained by the daily doses used in trial No. 1. Accordingly, 29 new volunteers were exposed for 5.5 days during July in two of the hyperendemic areas. Twelve of these were given an oral dose of 4.0 grams of chloramphenicol on the sixth, thirteenth, and twentieth days after the first exposure in the field.

Chloramphenicol given as a prophylactic measure to men exposed to scrub typhus in hyperendemic areas of the disease suppressed clinical evidence of infection during the 3 weeks that the drug was given and for from a week to 10 days after the last dose. Following this period the infection rates among the volunteers who had received prophylaxis in the 2 field trials were essentially the same as had been the rates in those persons who were exposed simultaneously and given a placebo. The disease in members of the prophylactic group was indistinguishable from that in the volunteers of the control group except for the prolonged incubation period and the lower incidence of eschar formation.

Two facts obtained from laboratory chemoprophylactic experiments, in which mice infected with R. tsutsugamushi were given chloramphenicol, are important in understanding the present results in human beings. It has been shown that viable rickettsiae were regularly recovered from the viscera of infected mice even though the animals were maintained for 3 months on daily doses of the drug which were sufficient to prevent the development of signs of the disease. The second point concerns the fact that reduction or elimination of fatalities can be accomplished in mouse experiments only when the drug is continued for at least 12 days after infection, and in some instances continued prophylaxis for 20 days is required. These observations in animals indicate that the drug does not sterilize the tissues of mice and that it must be given for a long enough time to allow the animal to develop its immune processes sufficiently to control infection at the time when the inhibiting agent is discontinued. In both of the experiments with human volunteers the suppressive effect of the drug was obviously lost before immunity had developed to an adequate degree.

In the present studies the suppressive effect of chloramphenicol on scrub typhus infection in man resembles that of atabrine on tertian malaria. If the observations on chemoprophylaxis of R. tsutsugamushi infections in mice may be applied to the prevention of scrub typhus in man, then it would appear that in the present work with volunteers the period of prophylaxis which was used was the minimum which might be expected to suppress the disease long enough to elicit a cure. Obviously, the present regimen was not successful in this respect. It is to be hoped that the prophylactic administration of chloramphenicol to men for longer periods after exposure may elicit the same

curative effect attributable to the adequate use of atabrine in infections with *P. falciparum* (malignant tertian malaria).

It is difficult to explain the absence of eschars in those who received prophylaxis and later contracted scrub typhus. Certainly the drug only suppressed the multiplication of *R. tsutsugamushi* because after its discontinuance the patients developed a generalized infection which was as severe as that which had been experienced by volunteers in the control group. It is possible that the absence of eschars indicates that an immune state was almost achieved as a result of antigenic stimulation from a subclinical infection before the suppressive effect of the drug was lost, and that local immune processes in the cutis were sufficiently well advanced to suppress the growth of rickettsiae there and, hence, to prevent the skin lesion from developing at the site of original inoculation of the agent.

Relapses have not been a feature of scrub typhus in man. Moreover, relapses were not observed in patients with the naturally acquired disease who were treated with chloramphenicol relatively early in the disease; the mean day for beginning therapy in these patients was 6.2. The high incidence of relapses (62 percent) in the volunteers in the first field trial was unexpected and disconcerting. That these were indeed recrudescences of the disease was indicated by the demonstration of rickettsemia in the majority of the patients during the first relapse.

In the first field trial the patients purposely were treated very early in the disease and usually received drug therapy for only one day. In view of this, the hypothesis which is looked upon as the most likely to account for the occurrence of relapses is as follows: the rickettsiostatic effect of chloramphenicol was dissipated within a short time after therapy was stopped. At this early stage of infection the immune mechanism of the host had not yet had time to respond adequately to the rickettsial agent. Therefore, after a temporary interruption due to drug, the growth of the rickettsiae proceeded at an unabated rate in certain of the patients. Finally, after an interval of from 5 to 10 days, the rickettsial multiplication reached a level sufficient to elicit clinical manifestations again. If such a hypothesis had a sound basis, one would expect that the occurrence of relapses would be related to the duration of the febrile illness prior to the beginning of therapy. The present observations do show a superficial correlation between very early treatment and the frequency of recrudescences of the disease. However, analysis of the data indicates that this apparent correlation might reasonably be due to chance. If the above hypothesis is considered, then it must be assumed that the initial short febrile period and the first recrudescence did not provide enough rickettsial antigen to elicit an adequate immune response in some of the patients, because a number of them had second and third relapses.

Two other factors which must be considered in discussing the relapses are (a) the size of the infecting dose of rickettsiae and (b) the relative resistance of certain strains of R. tsutsugamushi to control by chloramphenicol. The results of animal experiments indicate that with massive inoculations of rickettsial organisms one may break through the protective chemoprophylactic or chemotherapeutic effect of the drug. It is relatively certain that the volunteers in the first field trial had an unusually heavy inoculation of rickettsiae. It also has been noted that infections in mice caused by certain strains of R. tsutsugamushi are more readily controlled by chloramphenicol therapy than is the disease induced by other strains. Thus, chemoprophylaxis may be discontinued after 12 days when mice are infected with the Karp strain but this period of treatment is inadequate to protect the majority of mice infected with the Seerangayee strain. The latter do survive, however, when chemoprophylaxis is continued for a total of 20 days. Laboratory studies indicate that 3 of the strains isolated from the volunteers in the first field trial who suffered from relapses are as resistant to therapy as the classical Seerangayee organism which was recovered a number of years ago in Malaya. At this point considerable credence was given to the idea that relapses in the volunteers were associated with relatively resistant strains of rickettsiae. This hypothesis was discounted when it was found that 3 other strains recovered from patients without relapses, who had contracted their disease naturally in the same areas where volunteers were exposed, were as resistant to chloramphenicol as the strains isolated from the volunteers just mentioned. It would appear that the occurrence of relapses in the treated patients in the present work is probably dependent upon several unknown factors.

No evidence was obtained during the present work which would indicate that strains of R. tsutsugamushi readily acquire resistance or become fast to chloramphenicol. For example, those volunteers who received the drug as a chemoprophylactic measure over a period of 3 weeks and who subsequently developed scrub typhus responded as rapidly when the substance was given therapeutically as did patients with this disease who were given the material for the first time. Furthermore, when relapses occurred, they were promptly controlled by administration of chloramphenicol irrespective of how much drug the individual had received previously.

Ten volunteers had received experimental scrub typhus vaccine during earlier investigations because of possible exposure to infection. The vaccination did not influence the incidence of infection or the course of the disease in those persons developing scrub typhus. (Am. J. Hyg., July '49, J. E. Smadel et al.)

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Aureomycin in the Treatment of Pneumonia in Infants and Children:

In man, therapeutic doses of aureomycin up to 60 mg. per kilogram of body weight per day given orally have not been associated with toxic manifestations

except for occasional nausea, vomiting, and diarrhea. These symptoms have been transient and do not contraindicate or prevent continuation of therapy. Aureomycin is absorbed readily after oral administration, and the maximum rate of excretion in the urine occurs between 4 and 8 hours after the dose. Thus, an interval between doses of from 4 to 6 hours can be considered optimum. The oral route is the preferable mode of administration. Intramuscular injection is accompanied by local pain and sometimes induration and tenderness. Aureomycin may be given intravenously, but this method of administration was not employed in this series.

A study to evaluate the efficacy of aureomycin in the treatment of pneumonia in infants and children was instituted in January 1949. It has been found that strains of pneumococcus, streptococcus and Haemophilus influenzae are almost completely inhibited by aureomycin in concentrations of one microgm. per cubic centimeter or less. Such a blood concentration is readily obtained with therapeutic doses of the drug. Recently, Schoenbach and Breyer and Finland and his co-workers reported small series of cases of primary atypical pneumonia in which the patients responded well to aureomycin. This constitutes the first indication of any effective antibiotic agent in viral pneumonia, all previous therapy having been found to be ineffective. Thus, aureomycin, because of its versatility, seems to be an extremely valuable agent in treatment in pneumonia. A drug that is effective against both viruses and bacteria embraces a considerably larger antimicrobial range than either sulfadiazine or penicillin (or both combined) and should be effective against the vast majority of pneumonias encountered in the pediatric age group.

A uniform plan of study was employed in all cases, including nasopharyngeal and blood cultures, blood counts, x-ray examination of the chest, agglutinins for streptococcus MG and cold hemagglutinins at periodic intervals during the course of therapy. Nearly all the patients were seen in the follow-up clinic approximately 3 weeks after the onset of illness. At this time each patient was re-examined, and blood was drawn for follow-up streptococcus MG and cold hemagglutinin titers.

Examination of the flora of the nasopharynx has been reported to be a fairly reliable procedure in determining the causative agent of pneumonia in children. It should be remembered; however, that isolation of an organism from the nasopharynx is, at best, only partial evidence that it is the organism responsible for the disease in the lower respiratory tract. In the opinion of Alexander *et al.* the presence of substantial numbers of pneumococci in the nasopharynx of a child with pneumonia is a reliable index that the patient has pneumococcal pneumonia. The presence of a beta-hemolytic streptococcus or H. influenzae as the sole or predominant organism is only probable evidence that it is the pathogen in the lower respiratory tract. However, the isolation of hemolytic Staphylococcus aureus has little or no significance in determining

the etiologic agent in pneumonia because it is found so frequently in the naso-pharynx of normal children. A positive blood culture, of course, is presumptive evidence of the responsible organism of an associated pneumonia.

Thirty-nine patients fulfilling the established diagnostic requirements of pneumonia were studied. Their ages ranged from 3 months to 11 years. Aureomycin was administered both orally and intramuscularly. Oral medication alone was given to 25 patients. Nine received the drug intramuscularly, and 5 received it by both routes (but not simultaneously). Whenever possible, the drug was administered in capsules. In the younger patients who were unable to swallow capsules, the aureomycin was removed and one of the following vehicles was used depending on the likes and dislikes of the child: chocolate syrup, cherry syrup, applesauce, strained pears, lemon juice, orange juice, chocolate milk and jello. For the most part both infants and children accepted the aureomycin in spite of its disagreeable taste.

The daily dosage in the patients with bacterial pneumonias who were given oral medication ranged from 40 to 100 mg. per kilogram of body weight per day, with an average of 63.5 mg. The patients with viral pneumonias received from 25 to 65 mg. per kilogram of body weight per day, with an average of 45.5 mg. It should be pointed out that the latter group was composed largely of older children. No special attempt was made to calculate a precise dose of the drug on a weight basis. The drug was given orally in divided doses at intervals of from 4 to 6 hours. The intramuscular dosage varied from 3.0 to 12.0 mg. per kilogram per day, with an average of 6.5 mg., the drug being administered at 8-hour intervals. Aureomycin caused no untoward reactions aside from those referable to gastro-intestinal irritation. The triad of nausea, vomiting, and diarrhea occurred in 2 patients, whereas occasional vomiting without diarrhea was observed in 5.

Of the 13 infants and children who received intramuscular injection of aureomycin, 4 had a temperature drop to normal in less than 36 hours, and the temperature in 9 became normal after 36 hours. In comparison, 22 of the 26 orally treated patients had a normal temperature in less than 36 hours, whereas only 4 patients required more than 36 hours. Several of the infants treated by the intramuscular route showed tender, indurated buttocks, and this may have been a factor in the persistence of fever. It was the authors' impression that the oral mode of administration of aureomycin was superior to the intramuscular in its clinical effect in this series; hence, the intramuscular route was discarded early in the study, and thereafter employed only when it was impossible to give the drug by mouth. It is well to point out, however, that comparable doses of the drug orally and intramuscularly were not used, and therefore any rigid comparison between the 2 modes of administration would be untenable. Larger doses of the drug were not employed intramuscularly.

primarily because of the greater severity of local reactions with increasing amounts of the drug.

In the 30 patients with bacterial pneumonias treated with the drug, the results were considered good in 24, fair in 5, and poor in only one. The results were particularly good in pneumococcal pneumonia. Twenty-eight of the 30 patients were afebrile within 72 hours of initiation of aureomycin therapy. In the 9 patients with viral pneumonia treated with aureomycin, all but one were considered to have been favorably affected by the drug although the response was somewhat less striking than that observed in bacterial pneumonia. (New England J. Med., 25 Aug. '49, B. Olshaker et al.)

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Noradrenaline in the Adrenal Medulla: Noradrenaline, a primary amine differing from adrenaline only by the absence of an N-methyl group, has been regarded for some years as a possible chemical mediator liberated by adrenergic nerves. Lately, significant amounts of noradrenaline have been found in the adrenal medullas of cattle, and official American extracts of cattle adrenal medullas (U.S.P. epinephrine) have been shown to contain from 12 to 18 percent of this substance. These observations are not merely of academic interest, for adrenaline and noradrenaline differ significantly in their pharmacological actions. West has shown that noradrenaline is a stronger pressor agent than adrenaline, and cardiac-catheterization mentioned by Goldenberg *et al.* has indicated that although adrenaline acts as an over-all vasodilator and causes hypertension only by increasing cardiac output, noradrenaline acts as an over-all vasoconstrictor with no change or a slight reduction in cardiac output. The metabolic actions of these substances also differ, the hyperglycemic effect of noradrenaline being much less than that of adrenaline (ratio 1:8).

Goldenberg and colleagues believe that as long as the noradrenaline content of the adrenal medullary secretion is constant at, say, 18 percent then present concepts of adrenal secretion are fully valid because small quantities of noradrenaline would not significantly alter the functions of adrenaline. But the noradrenaline content of the adrenal medullary secretion may increase under pathological conditions, and Holton has recently reported large amounts in 3 cases of adrenal medullary tumor (pheochromocytoma). Profound alteration of carbohydrate metabolism and of the usual hemodynamic effects of the adrenal medullary secretion may be expected in such cases; and if, as Goldenberg *et al.* suggest, under varying physiological conditions the noradrenaline content of the adrenal medullary secretion varies widely, current views of the physiology of the adrenal medulla may have to be considerably modified. (Lancet, 16 July '49, Annotation)

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Some Principles of Fly Control: By the use of DDT to supplement sanitation, flies may now be brought under control in homes, restaurants, food markets, and all food industries. Effective fly control, whether insecticidal or cultural, must be based on fly habits.

The objective in DDT spraying for fly control is to leave a thin coating of DDT crystals on those surfaces which flies frequent. This film kills the flies through contact alone, so that if the favorite resting-places of flies are treated, an effective control may be obtained. Because flies rest at night and are active only in the daytime, spraying their nighttime resting-places insures the greatest contact time and heightens the control efficiency of the DDT deposit.

The accepted dosage level for DDT spraying is 7 ounces of DDT deposited per 1,000 square feet of sprayed surface. This rate, also termed 200 milligrams per square foot, is high enough to allow for many of the inaccuracies of spraying technic. On interior surfaces this dosage usually remains actively toxic to flies for 3 or more months. Outdoors, subjected to attack by the elements, it degrades far more rapidly.

In most instances where sanitary conditions are generally acceptable, the use of DDT as a residual deposit on interior surfaces alone is adequate for good fly control for about 3 months, but occasionally the breeding area or fly source is too great and overwhelms the effectiveness of this residual spray. This happens most frequently in industrial plants which have animal or vegetable wastes that are not given prompt disposal. Such conditions commonly occur in feed mills, slaughter houses or abattoirs, fat-rendering plants, hide and fur establishments, seafood plants, and canneries.

DDT-kerosene solution or DDT-Triton-xylene emulsion are the usual spray materials used on interior surfaces. As the amount of liquid absorbed by such surfaces varies greatly, it has been considered best to vary the percentage of the final spray dilution according to the type of surface and still maintain the same spraying technic, thus guaranteeing adequate dosage of DDT in spite of this variation in absorbability. In general, the proper criterion for spraying is to wet the surface thoroughly, but without run-off due to droplet coalescence. With this practice the proper dosage is applied if a 2-1/2-percent spray is used on rough unpainted wood surfaces such as those found in dairies and other farm buildings, a 5-percent spray used on well-painted or plaster surfaces such as those in markets and industrial plants, and a 7-1/2-percent spray used in restaurants and homes having smoothly finished surfaces. On surfaces with which special care of the finish is unnecessary, some degree of run-off may insure adequacy of treatment, but any run-off leaves visible streaks on varnish and other decorative finishes.

The most efficient equipment for DDT-residual spray application is a low-pressure sprayer, either the hand-compression garden sprayer, a hand sprayer with an air-pressure tank and filler valve, or a machine-operated pump sprayer. With this equipment a fan-pattern spray nozzle should be used at a pressure of from 35 to 60 lb. per square inch. For fine surfaces, a flat atomizing spray nozzle having a 50° fan and delivering 0.15 gallons per minute at 40 lb. pressure can best be used for the 7-1/2-percent spraying on fine surfaces. For the 5-percent spraying on painted and plaster surfaces, the 50° fan nozzle with a 0.2 gallon per minute output is satisfactory, although for dairy spraying the 50° nozzle with the higher delivery rate of 0.4 gallon is more efficient.

For outside treatment of fly resting-places, the wettable DDT compounds are probably better than solutions, as they are not as likely to be harmful to plants, and furthermore they appear to adhere more readily to exterior surfaces and to trees, grass, and bushes. In some instances, emulsions have been heavily applied to plants with no damage, but oil solutions are certain to burn foliage badly. It may be best to apply a 5-percent DDT spray on exterior surfaces, and use a fan spray nozzle having 0.4 gallon per minute output. A higher dosage is consequently applied to cover the unknown values of weathering and adhesion of the spray residue.

Flies multiply with incredible rapidity, and with favorable conditions they reach astronomical numbers in a few generations. The eggs hatch in a day's time or less, the maggots mature in roughly a week, and then transform in the pupal stage to produce the winged adult, often all in as short a time as 10 days. The adults mate and feed, seek out garbage, manure, or other waste, and as their eggs mature, the females lay them by the hundred, starting the cycle over. The larvae or maggots require air for breathing, so they can live only on the surface of very wet material, but will readily penetrate moist but solid media to a depth of several inches. When mature, the maggots crawl into the nearest dry place of concealment to pupate or transform, there to stay motionless for a few days until the newly developed adult breaks its way out of the pupal shell. As places satisfactory for pupation may not be present in their breeding medium, maggots often migrate many feet away from wet breeding areas to pupate under the most accessible dry trash.

In control work it must always be borne in mind that flies breed freely only in moist media furnishing a fairly substantial amount of nutrient material. Vegetable waste low in usable carbohydrate or protein, food debris of any kind dried out or scattered, food substances greatly diluted by soil, or other inert material are of no consequence, but even a small handful of moist rich manure, stock feed, restaurant scraps, offal, or other material with a high protein or available carbohydrate content will turn out a surprising number of flies, often several hundred per pound. The adult flies live for several weeks, so a constant but small source of flies may build up a large adult population around a given premise.

Before initiating fly control, one must consider the kind of fly which is responsible for the particular problem, in order to proceed most efficiently with a program of cultural sanitation or DDT treatment. Blowflies (calliphorids), generally considered as the green and blue bottleflies, show many characteristics that separate them from houseflies with regard to their breeding habits, and consequently their control by DDT and sanitation methods. It has been generally observed that if an establishment has no attractants (or breeding places) for blowflies, it has no blowfly population. Blowflies seem to range over a wide area, and in this respect an analogy can be drawn between them and vultures, for a premise may be immaculately kept and have no blowflies, yet if attractant food substances are exposed, a sizeable blowfly population can build up within an hour, the flies having stopped there in their ranging about for food and suitable breeding media. Blowflies prefer not to enter buildings, in contrast to houseflies. In most areas blowflies are more efficiently controlled on a vicinity-wide basis than on a single premise. House flies are very domiciliary, for they tend to stay within a restricted locale and to go inside buildings, especially to rest there overnight in cool weather. They leave their home areas only by accident or by being forced out through the competition of their own numbers. For this reason housefly control may be effective on as small a scale as a single farm, residence, or business. It is then apparent that although housefly control may be successful on a given premise if flies are not overflowing into it from other premises, blowfly control must always be done on a vicinity basis. However, in abattoirs, seafood plants, canneries, and food processing plants, the blowfly problem may be primarily one of the plant itself.

To insure the efficiency of a control program for flies, or of even a single DDT application, it is of the utmost importance to conduct fly resting-place studies at night to determine where the DDT should be applied. When one considers that because flies are inactive at night, and so rest for several hours in the same spot, and that a DDT application either of a very low dosage or of long-standing (subjected to erosion and degradation by the elements) would be lethal because of such a prolonged contact time, the importance of treating as much as possible of the nocturnal resting-areas becomes apparent. Treatment with reference to just those daytime resting-places on which the flies spend but a very brief period undoubtedly gives control, especially if the treatment is recent or the dosage high; but such a method may neglect a majority of the nocturnal resting-areas and so be unable to compete in rate of kill with the rate at which the flies are emerging from their breeding places.

Studies of resting flies in various areas at night have revealed an interesting variety of preferences. At night during warm summer weather houseflies as well as blowflies rest outdoors, sharing similar resting-places near their major daytime centers of activity about garbage, manure, privies, stables, and kitchen entries. In cooler weather the houseflies tend to rest inside buildings

on ceilings and other overhead structures, although the blowflies continue to choose outside resting-places. Flies show even more gregariousness in their choice of nocturnal resting places than in their daytime activities, a point of distinct value in DDT-residual control work, because this characteristic makes it possible for the control measures to be focused on a greatly reduced area, thereby increasing efficiency and economy.

The nocturnal outside resting-places of flies seem to possess several characters in common. They are generally places which are: (1) within 20 feet of the most favored daytime feeding and breeding areas; (2) exposed or prominent in position as vantage points, such as twigs on the ends of low branches, fences, clothes lines, or electric wires, edges or margins of building structures, outer leaves of weeds and low bushes, and isolated weeds taller than the surrounding herbage; (3) protected from direct wind, but still open in situation even if the weather is not calm; (4) above the actual ground level, but rarely more than 15 feet in elevation. Observations made on houseflies resting inside buildings at night have always shown their preferences for edges and prominences which doubtless is the underlying principle of their resting behavior outside. Because of these nocturnal resting-habits of houseflies, the emphasis in all interior DDT-residual spraying must be placed on adequate treatment of overhead structures, such as light wires, cords, edges of beams and other woodwork, and all irregularities in the ceiling structures.

Because a given premise having large quantities of fly-infested food waste may easily become full to capacity with adult flies, and in addition have unseen hordes overflowing to other premises, good control measures, even though effecting an appreciable reduction in this outflowing fly population, still may seem to better the premise conditions but very little because the control must cut down most of the overflow before its effect becomes of value locally. For this reason it is often possible to have some control over the fly output of an abattoir or packing plant without obviously benefiting the plant itself.

The total control effect exerted by DDT-residual spray measures is of course limited in any instance to the total amount of fly resting-area that can be treated. If all resting-areas in and about a given premise are wholly treated, it follows that because the total capacity of those surfaces is the limit of such control measures, the flies produced in excess of such a capacity go uncontrolled. This uncontrolled amount, the unseen output of an area of heavy fly breeding, simply keeps the resident population replaced as fast as it is killed off, leaving no apparent control value, but in reality suppressing the overflow which had been migrating to other areas. If real control value is to be achieved at the focus of extreme fly breeding, then measures in addition to the DDT-residual treatment must be employed to reduce the volume of breeding. Proper waste disposal or larvicing are therefore necessary to assist the DDT residual in reducing the number of adult flies below the level of premise capacity. Under

conditions of fly breeding in excess of the capacity of a premise for adults, it has been observed that all conceivable breeding places become infested, most of which never would have been chosen for oviposition by a fly population below the capacity level. As examples, moist dirty linen from restaurant tables, scraps of food hidden in boxes in restaurant storerooms, collections of food trash on the floor, and soil damp with garbage liquors have been found heavily infested with maggots. In these instances a high population pressure had forced oviposition in situations ordinarily not chosen, creating a far more difficult control problem.

The importance of getting the upper hand in fly control cannot be over-emphasized, for the ovipositing behavior of houseflies depends on their population pressure (the degree of competition based on the extent to which flies saturate the breeding capacity of the premise). Houseflies are so very gregarious during their oviposition, that there is a definite tendency for a group of egg-laying females to infest certain chosen points as their breeding sites to the fullest, disregarding certain other adjacent areas which appear equally suitable. The number of such sites infested by a small fly population is usually limited to a very few of the most choice, although a very large population saturates all available sites. Although the breeding places of a small population are therefore fewer in number, they nevertheless are still heavily infested, instead of being scattered, numerous, and lightly infested. For the reason that the fly population is self-restricting in breeding area, a light population is far easier to control, and is particularly adapted to check by a well-placed DDT-residual treatment, which can exercise such efficient control that only a few of the potential areas available later become infested. If the fly population is allowed to increase to the point at which it infests all potential breeding places, then the fixed area treated by the DDT-residual may be inadequate for control of more than a small percentage of the flies, and so have no suppressive effect at all on the extent of breeding. Consequently, the initiation of fly control early in the season, or at a time when flies are least numerous, tends to restrict the breeding to fewer places and so make control easy to maintain.

The flight range of flies, especially of houseflies, has often been studied, but the factors underlying fly migration and the degree to which it figures in their control are still not well understood. It is definite that flies under certain circumstances, especially under conditions of high population pressure, can and do migrate over areas up to a few miles in extent. The migration of both houseflies and blowflies out of areas of high population pressure, such as may exist about poorly sanitized industrial plants and city dumps, is usually the reason for a high fly index over an entire municipality. Consideration of these factors of fly migration makes it apparent that the control of heavy breeding areas is of singular importance, for not only are such measures of local value, but even more important, they remove the sources of over-all fly infestation for surrounding areas.

One of the most common causes of very high fly population about dairies arises from the poor handling of stock feed rather than inadequate manure disposal. A high protein stock feed, if allowed to become moist by spillage on the ground in handling, feeding stock, or even sifting through floors or feed troughs, has been found to create phenomenal fly populations, the source of which is often very difficult to discover. The conditions necessary for house-fly breeding are primarily the presence of a fairly high protein or available carbohydrate, which means that the general debris about a farm will not support fly breeding. It has been found that the ordinary low-grade type of barnyard, knee-deep in filth, may produce relatively few flies because the dirt and manure mixture is very low in available food. However, attendant upon such conditions as these, there are certain malpractices that are responsible, and which have been consistently overlooked in the face of more obvious sanitation failures. The old and classical manure pile has always been a notorious source of flies. Any method of spraying it to control flies is not only uneconomical, but also would be an attempt to support this out-moded and, in most areas, outlawed practice. However, a common substitute, that of temporary manure storage, may often breed as many flies, especially if the manure is left out in the open, and is removed only twice a week or even less often. Teeming cultures of fly maggots are commonly observed in manure spreaders left standing a few days for each load. Temporary manure storage on the ground is especially guaranteed to give trouble as the maggots may mature in a very few days, to complete the rest of their development in the soil, so that removal of the manure at regular intervals may not be enough. The construction of field storage piles is often too close to the dairy. Several hundred feet, considered by many to be sufficient distance, is definitely unsatisfactory if the manure is not hauled there daily, for in keeping it in the barnyard it becomes heavily infested, and the flies which emerge later in the field storage pile find their way to the barn. Although not always practical, cow manure can often be stacked in small piles in a dry barnyard, with reduced breeding resulting, for the surface soon dries over and becomes unattractive to the egg-laying females. It is for this reason that houseflies rarely breed in individual cattle droppings. After cow manure has lost much of its moisture and has become solid, it is the source of but few house flies, although it will produce goodly numbers of stable flies.

An odd, and perhaps infrequent, source of flies in dairies is in the cattle urine pits formed in the earthen floors of resting-barns or holding-sheds. These depressions are roughly 3 feet across and are kept wet by regular use. They contain urine-soaked soil, with but little manure, and strangely do show heavy housefly infestations.

One of the most favorable media for fly breeding is horse or mule manure, which may support several hundred maggots per pound. Stable floors should be solid, and so constructed that the manure can be removed daily by scraping and shoveling. Deep litter is very likely to harbor heavy infestations, especially if

the substrate or the ground is moist. All other stables, whether for calves, bulls, or freshening cows, represent potential fly hazards, but DDT treatment of these places satisfactorily controls their fly output.

Chicken houses, hog pens, and other livestock quarters interfere seriously with efforts to control flies with DDT on the dairy farm only if the sanitation of these places is grossly neglected, or often more important, if the rich feeds used are allowed to mix with the manure, soil, or otherwise become available for fly breeding.

By far the majority of flies in a restaurant are houseflies, which come in from the streets, either by way of the front entrance, or more generally, through the alley door. In facing the problem of fly control in food establishments, a study of the environment is often necessary to reveal the source of the flies, which can be great enough to cover up the efficiency of a DDT treatment. Open front shops are so dependent upon the sanitation of the surrounding area, that DDT can exercise only limited control, but still be superior to space sprays, which are definitely at a great disadvantage in such shops. Any garbage station that is not kept clean and is irregularly serviced will be a prime source of flies, but an apparently well-kept garbage station may also be a source of a great number of flies, even though all litter be removed and the area washed daily. If liquid food wastes, or wash water containing food, is allowed to seep into soil, whether between bricks of a street, under platforms or under a few inches of gravel, the requisite conditions for fly breeding are set up. Blowflies will always breed in garbage cans which are not emptied and cleaned regularly, and if so neglected, will be produced in enormous numbers if fish or meat waste is left undisposed in such cans for a very few days. The full grown maggots crawl out of the cans and pupate in the nearest available place of concealment. The source of flies for one large cafeteria was discovered to be in the loose soil and rubble under the rear loading platform. Enough food scraps, water, and other debris fell through the wooden grating of the platform to support a sizeable fly population.

In general, those food establishments that either lack alley entrances or use them infrequently have less trouble with flies. The best procedure under a heavy fly infestation is to keep such an entrance locked and keep all garbage inside and covered, removing it but once a day. It has been observed that restaurants routinely keeping their garbage inside, even uncovered, have fewer flies than those that place it in the alley and use the alley door frequently. With proper handling of alleys by both the restaurateurs and the municipal disposal services, there would be few fly problems in restaurants. Ventilation systems may produce such a strong negative pressure at the back door, that every time an employee uses this entrance, the flies are literally blown in from the alleyway despite a double-door system. Placing of intake fans on a level with the street is not advised because many flies may be drawn in with the air stream. Air-conditioning systems often keep out flies during their operation simply because

the restaurant doors are then allowed to remain closed, and the cool dining room is no longer as attractive to the flies; however, the kitchen of such a restaurant may continue to be as infested as ever.

There are several specific places in a restaurant kitchen that may support fly breeding. One of the least obvious is the accumulation of stove scrapings between and behind steel stove grills. Rather astounding deposits several inches in depth and of long-standing have been discovered. The base of a food elevator or dumb waiter often collects a great amount of spilled food and trash, affording conditions favorable to flies, particularly if floor flushing or mopping keeps the material moist. An old cracked meat block may be a breeding place for flies; blocks have been observed with from 1/4- to 5/8-inch cracks filled with putrefying meat scraps and juices. In one hotel kitchen having a very high fly population, overlooked dirty dishes containing leftover food were found to be heavily infested with maggots. In another restaurant extremely dirty linen was also found heavily infested.

Food which falls behind or under cabinets, bars, soda fountains, or other inaccessible places may be responsible for some flies, particularly with the practice of floor flushing, as this keeps the debris moist. For this reason restaurant floors should be accessible over their entire surface, to make complete cleaning possible. Cabinets, bars, or enclosed counters which rest almost flush with the floor, but still allow dirt, trash, and food scraps to accumulate under them, not only favor flies, but also rats, roaches, and other vermin.

In far too many instances soda and ice cream counters are very insanitary. The slime of milk residue and debris of food scraps which may accumulate in them is the cause of the spoiled milk odor so prevalent in lower-grade drug stores and ice cream parlors. Such conditions not only make fly breeding possible but actually support an annoying population. Faulty construction and ignorance of thorough cleaning procedure for more complex equipment is responsible for many flies. Milk residues are highly attractive to flies, and nutritious enough to support them in large numbers.

The fly problem of an eating establishment may even be a vicinity matter, one of unfortunate location for the restaurant. Suburban locations in unrestricted areas are often much too close to riding stables, stock farms, or meat processing plants, whose overflowing fly populations are difficult for the restaurant owner to curtail; he can only exercise great strictness in his own sanitation in an attempt to reduce the number of flies which will be attracted to his particular establishment. The conditions of a generalized housefly outbreak have a pattern similar to that of blowfly populations. Under such conditions the need for community action to protect the eating establishments and residences from flies is quite clear. More often though, the individual restaurateur can adequately handle his own fly control with good sanitation and DDT spraying.

The problem of housefly and blowfly control in industrial plants often ceases to be just a small part of their sanitation program, especially when great quantities of industrial waste are available for fly breeding. Feed mills, canneries, vegetable packing houses, abattoirs, hide and fat-rendering plants, fruit juice factories, and many other such concerns have major fly control problems, yet need but little instruction about the source of their flies. Their need is for a conscientious and well-directed effort in reducing fly breeding, in addition to which the methods of DDT fly control that have been discussed will serve as important adjuncts.

In some industrial establishments the cause of large fly populations may often be rather obscure, as for example, in fat-rendering plants. In this industry not only is fly-proof waste disposal of paramount importance, but special precautions must also be taken to guard against soil contamination, which is a far greater factor than that for dairy feed and garbage handling. Around many fat-rendering plants the soil is allowed to become partially grease-soaked for the top few inches, creating an excellent medium for blowfly breeding. Plants have been studied in which many square feet of soil about work platforms were literally alive to a depth of a few inches with blowfly maggots. Upon examination the soil was found to be free of any debris, and appeared quite like ordinary earth, except for its strong odor and greasiness. Although the use of DDT as a substitute for good sanitation is certainly possible to a disturbing extent, such a policy is most deplorable, and should be condemned by the plant manager as well as the sanitation officer. Those DDT technics which have been found effective for dairies, restaurants, and meat or seafood markets are applicable in general to the manufacturer's problems; but to achieve a similar degree of control over flies, good sanitation must accompany these methods, and in particular, far better disposal services than are generally provided in practice. Without these, the use of DDT sprays in plant buildings may achieve very little. (Am. J. Trop. Med., July '49, H. L. Scudder)

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Study on the Control and Biology of the Housefly in the Middle East: In laboratory tests chlordan and methoxychlor outlasted DDT as a residue on mud-brick surfaces. Chlordan appeared to be the best of the 3. Between the seventh and eighth weeks after application, however, methoxychlor was more effective than the other 2, when the contact period was reduced from 2 hours to one minute.

Benzene hexachloride deposits as heavy as 100-200 mg. of the gamma isomer per square foot retained their toxicity longer than a 200 mg. DDT treatment. By the eighth week, DDT was no better than 50 mg. of the gamma isomer as a knockdown agent.

Chlordan, methoxychlor and DDT were also applied to the walls and ceilings of occupied mud homes. Housefly counts that were made in these

buildings before and after treatment showed that chlordan substantially reduced the infestation for at least 4 weeks. A gradual reduction also occurred in those treated with DDT and methoxychlor but counts made in untreated buildings indicated that a normal seasonal fluctuation rather than the insecticides may have been responsible for most of the results obtained. Only chlordan appeared to give adequate control.

From 4 to 4-1/2 weeks after application houseflies were exposed under Petri dishes on the walls and ceilings of the structures treated with DDT and methoxychlor to find out if a toxic residue was still present. Knockdown times comparable to those recorded in laboratory tests with 200 mg. deposits on mud panels occurred on 10 of the areas selected. In 4 cases, however, the wall deposits were less effective than the panels.

After observing that houseflies tend to rest outdoors on vegetation rather than indoors on warm summer nights, a DDT water wettable spray was applied to the trees and bushes in the village of Moneeb. Although the treatment appeared to have considerable effect on the number of flies present, a greater reduction will be required before the control can be considered satisfactory.

A study of the influence of time of day and temperature on adult emergence revealed that houseflies emerged on a rising temperature and that most of the emergence occurred between 76° and 90° F. During June and July, these temperatures prevailed in the morning between the hours of 0700 and 1100; very little emergence occurred between 1200 and 2400. Peak emergence in 2 tests took place when the air temperatures were 81° and 84° in the 2 tests respectively. Over 50 percent of the total emergence took place within a 4° hourly rise in temperature.

In a comparison of various kinds of dung as larval media, it was found that maintenance of original moisture content by daily addition of water was advantageous to the percent of fly emergence with camel, sheep, and cow dung, made little difference with donkey or pig dung and was detrimental with NAIDM media and horse and pig dungs, and slowed down the rate of development of larvae feeding in camel, cow, gamoose, and sheep dungs. The daily addition of water to horse, cow, and sheep manures produced larger flies than the same materials unwatered; among the other materials little difference was shown.

A value determined by multiplying the percent emergence by the size of the prothorax of flies was used as an index of the efficacy of the dungs as larval media. According to this value the dry media rank as follows: NAIDM media, human feces, and the dungs of pig, horse, cow, sheep, gamoose, camel, and donkey. When the media were wet the order was somewhat different: NAIDM media, pig, cow, sheep, horse, camel, gamoose, human and donkey. (Res. Proj. NM 005 034, Branch No. 713, Rep. No. 4, Nav. Med. Res. Unit No. 3, Cairo, Egypt, 8 Aug. '49, J. B. Gahan et al.)

List of Recent Reports Issued by Naval Medical Research Activities:Naval Medical Research Institute, NNMC, Bethesda, Maryland

<u>Project</u>	<u>Report No.</u>	<u>Date</u>	<u>Title</u>
NM 004 001	4	16 Jun '49	Considerations Underlying the Use of Ultrasound to Detect Gallstones and Foreign Bodies in Tissue
NM 005 004 (X-535)	22	4 May '49	Variations in Infectivity of Cercariae of <u>Schistosoma Mansoni</u>
NM 005 020	2	19 May '49	The Orthopodomyia Anopheloides Subgroup of Mosquitoes (Diptera: Culicidae)
NM 007 024 (X-759)	6	13 May '49	The Nonspecific Inhibition of the Lecithinase Activity of Type A <u>Clostridium welchii</u> Toxin
NM 007 025	4	28 Jun '49	The Experimental Use of Homogenous Vein Grafts to Circumvent the Pulmonic Valves
NM 007 039	21	7 Apr '49	The Response of the Peripheral Blood of Swine to Whole Body X-Ray Radiation in the Lethal Range
NM 007 039	22	14 Jun '49	The Effect of Total Body X-Radiation on 17 Ketosteroid Excretion in Dogs
NM 007 040	3	10 Mar '49	Retention of Amino Nitrogen in the Plasma Following Surgery - Further Studies
NM 007 047	3	28 Apr '49	Factors Influencing the Production of Fever by Influenza Viruses in Rabbits

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Naval Medical Research Institute, NNMC, Bethesda, Maryland (Cont.)

<u>Project</u>	<u>Report No.</u>	<u>Date</u>	<u>Title</u>
NM 007 047	4	3 May '49	Tolerance in Rabbits to the Pyrogenic Effect of Influenza Viruses
NM 008 002 (X-418)	9	19 May '49	The Effects of Standard Diets and Some Concomitant Variables on the Incidence of Dental Caries in White Rats
NM 008 009	1	3 May '49	Distribution of Radioactive Gallium in the Teeth and Jaws of Experimental Animals
NM 011 013	6	12 May '49	The Biological Significance of Radiogallium (Ga ⁷²)
(MR-49-4)		30 Jun '49	A Comparison of the Constant and Instantaneous Injection Techniques Using T-1824 for Determining Cardiac Output

School of Aviation Medicine and Research, NAS, Pensacola, Florida and Tulane University, Louisiana

NR 140-155	1	1 May '49	The Relationship Between Apparent Displacement and Motion in the Oculogyral Illusion
NM 001 002			Post Rotational Auditory Localization
NR 140-455	2	13 May '49	
NM 001 002			The Delay in Visual Reorientation Following Exposure to a Change in Direction of Resultant Force on a Human Centrifuge
NR 140-455	3	12 Jun '49	
NM 001 037			
NR 140-455	4	3 Jun '49	The Perception of the Postural Vertical
NM 001 037			Report No. 1: The Modification of Nonlabyrinthine Cues
NR 140-455	6	21 Jun '49	The Perception of the Vertical III. Adaptation Effects in Four Planes
NM 001 037			

School of Aviation Medicine and Research, NAS, Pensacola, Florida

<u>Project</u>	<u>Report No.</u>	<u>Date</u>	<u>Title</u>
NM 001 045	3	17 May '49	The Relationship of External Pressurizing Systems of Anti-Blackout Suits to the Formation of Edema and Petechiae
NM 001 048	1	25 Jul '49	The Effect of External Fluid Pressure During Positive Acceleration Upon the Respiratory Rate, Pulse Rate and Right Intra-Auricular Pressure of Rabbits

School of Aviation Medicine and Research, NAS, Pensacola, Florida and Kenyon College of Gambier, Ohio

NR 872 004	1	21 Jul '49	Rate of Speaking I. Relationship Between Original and Repeated Phrases
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Medical Field Research Laboratory, Camp Lejeune, N.C.

NM 005 044	-	10 Aug '49	The Mosquitoes and Mosquito-Borne Diseases of New Caledonia
NM 011 021 (Sub-Proj. 11-49)	-	10 Jun '49	Packaged Iodine, Freezing Point
NM 011 021 (Sub-Proj. 15-49)	-	17 Jun '49	Testing of Portable Gasoline Driven Insecticide Sprayer
NM 012 011	-	23 Jun '49	Evaluation of Disinfectants for Cold Sterilization Purposes

Note: Those interested in seeing copies of the complete reports should address their request to the research activity from which the report originates.

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Note on Motion Sickness Tablets (Dramamine): Motion Sickness Tablets, 100 mg., scored, (Dramamine) (see News Letters of 22 April 1949 and 17 June 1949) are being recommended to the Armed Services Medical Materiel and Specifications Committee for standardization as a catalog item.

In the study made by Gay and Carliner aboard a troop transport, dramamine was administered in a dosage of 100 mg. every 5 hours and before retiring. When a patient was unable to retain a capsule orally, he did retain and absorb the drug when administered rectally. The results following the rectal administration of dramamine were as rapid in occurrence and as complete as those derived from its use orally. Satisfactory prophylactic and therapeutic effects may be obtained in some persons by the use of 50 mg. per dose, for a total of 200 mg. instead of the 400 mg., as above.

Although the synthesis of dramamine (benadryl plus 8-chlorotheophyllin) was designed to eliminate drowsiness as a side reaction of the antihistaminic base, some drowsiness may result from its use. Because of this, dramamine should be used with particular care for duty personnel aboard ships, aircraft, etc.

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Disestablishment of the U. S. Naval Hospital, Corona, California: In a recent letter to the Secretary of the Navy, the Chief of BuMed recommended that the U. S. Naval Hospital, Corona, California, be disestablished as of 1 November 1949. Medical care for all patients currently treated at Corona can be provided in the naval hospitals located at Long Beach and San Diego.

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Course in Venereal Diseases for Medical Officers: The Thirteenth Venereal Disease Postgraduate Course under the sponsorship of the U. S. Public Health Service is to be given at the U. S. Public Health Service Medical Center, Hot Springs, Arkansas, from 31 October through 5 November 1949. The course consists of a daily series of lectures covering all phases of each venereal disease, and in addition includes education of the patient in this regard, case finding and follow-up, case presentation, and contact interviewing.

Requests are desired from all medical officers interested in participating in this course. To receive consideration, requests must reach BuMed by 15 October 1949 and may be made by dispatch if the time element involved requires such action. Requests submitted by dispatch must be confirmed by a following letter. Authorization orders only will be furnished in accordance with Joint Letter 49-412 of Navy Department Bulletin dated 31 May 1949. No reliefs will be provided for attending medical officers. (Professional Div., BuMed)

Training Duty for Reserve Dental Officers: Training duty for approximately 43 Volunteer Reserve dental officers from all sections of the continental United States will be available at the Naval Dental School, National Naval Medical Center, Bethesda, Maryland, during the period of from 7 to 19 November, inclusive. This duty will consist of training in professional and military subjects appropriate to dental officers and a one-week course on the medical aspects of special weapons and radioactive isotopes, which will be held jointly with Naval Reserve medical officers. Inquiries regarding this training duty should be addressed to the cognizant district commandant - Attention: District Dental Officer. (Dental Div., BuMed)

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General Course of Instruction for Dental Officers of the Regular Navy

and Naval Reserve: Two General Courses of Instruction for dental officers have been completed recently, one at the Naval Training Center at San Diego, California and one at the Naval Training Center, Great Lakes, Illinois. These courses are of 14 days' duration and consist of lectures, classroom instruction, and practical training in military close order drill and firearms, including firing on the range. Nineteen dental officers, 9 of whom were of the Naval Reserve on active duty, completed the course at San Diego on 30 July. Eighteen dental officers completed the course at Great Lakes, graduating on 19 August; in this class there were 2 officers of the regular Navy, 6 of the Naval Reserve on active duty, and 10 of the Naval Reserve on inactive duty.

Further information on this course may be obtained from the cognizant district commandant. (Dental Div., BuMed)

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Request for Back Issues of Medical Periodicals and Publications: The Bureau of Medicine and Surgery is sponsoring a group of German scientists engaged in the preparation of an Atlas of Epidemiology. One of the essential needs is a library of American medical periodicals and literature for the period from 1939 to 1949. It is the desire of the Bureau of Medicine and Surgery that medical officers and others possessing copies of medical journals, listed below, forward them to BuMed, Code 7211, if no longer needed:

1. American Journal of Hygiene
2. American Journal of Tropical Medicine and Parasitology
3. Journal of Experimental Medicine
4. Journal of Infectious Diseases
5. Journal of Hygiene
6. Journal of Parasitology
7. Journal of Tropical Medicine and Hygiene
8. Southern Medical Journal

BUMED CIRCULAR LETTER 49-100

17 August 1949

To: BuMed Management Control Activities (as indicated)

Subj: Fiscal Work Measurement ProgramEncl: 1. Definitions and Reporting Instructions
2. Sample Report Form

This letter states that the Fiscal Director of the Navy Department, in accordance with instructions of the Secretary of the Navy, has prescribed a work measurement program for fiscal work in the Department of the Navy. Enclosure 1 contains definitions and reporting instructions to be followed by addressees in preparing monthly reports for submission to BuMed. Data in these reports will be consolidated by BuMed before being transmitted to the Fiscal Director, Navy Department. The consolidated reports will be used to meet requirements of the Bureau of the Budget in the formulation, justification, and evaluation of budget estimates and to show fiscal functions in need of improvement. The first reports are to be for the months of July and August 1949 and will be due on or before 15 September 1949. Reports for succeeding months should be submitted to reach BuMed within 15 days after the end of the month being reported.

In addition to this fiscal work measurement program, a number of similar programs are expected to be put into effect in the near future, covering functions which are considered common to all activities of the Navy Department. These programs are designed to collect data to formulate, justify, and evaluate budget estimates for transmission to the Bureau of the Budget, Executive Office of the President, to determine and justify civilian personnel ceiling estimates, and to increase operating efficacy by pointing out those areas where improvements can be made.

The letter further states that some of the greatest benefits of these programs may be realized at the activity level through careful analysis of the data collected monthly and by comparison with previous reports. Staffing problems, functions in need of improvement, etc., can be determined through such analysis and comparison and definitive remedial action taken.

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BUMED CIRCULAR LETTER 49-101

18 August 1949

To: Commandants, All Naval Districts and River Commands

Subj: Civil Death Certificates: Procurement and Payment for

Refs: (a) Comptroller General ltr, A-39800 dated 17 December 1931 to the Secretary of the Navy
 (b) Paragraph 3411, Manual of the Medical Department
 (c) Paragraph 56308, BuSandA Manual
 (d) BuMed Cir. Ltr. 48-48

This letter cancels reference (d) and states that (1) all civil death certificates required for the official use of the Navy Department, regardless of the category of Naval or Marine Corps personnel involved, are properly chargeable to the appropriation, "Medical Department, Navy," (2) in the event advance payment is required, the prepayment of the legal fee may be made from the personal funds of an officer by cash or any negotiable instrument as may be acceptable to the various state, county or city authorities as directed in reference (b), (3) reimbursement for these prepayments will be made by the local disbursing officer to the personal funds of the officer providing the cash and/or obtaining the acceptable negotiable instrument in the amount of its face value plus any service charge in accordance with instructions contained in reference (c), (4) the Bureau of Supplies and Accounts authorizes local supply officers to request authority from that Bureau to establish a spot cash purchase fund for the purpose of making cash advances to officers for over-the-counter transactions, (5) at activities where local supply officers have authority and have established such a fund, (2) and (3) above need not apply, and (6) arrangements should be made with the local supply officer in obtaining advances.

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BUMED CIRCULAR LETTER 49-102

18 August 1949

To: All Ships and Stations

Subj: Object and Subobject Classification of Medical Department Appropriational Estimates, Obligations, and Expenditures.

Ref: (a) BuMed C/L 45-178 of 7 July 1945; AS&SL July-Dec 1945, 45-801, p. 342; and NavMed 855.

This letter states that because of recent changes in Budget-Treasury Regulations No. 1 effective 1 July 1950, certain changes will be made in ref (a). See 31 August 1949 Navy Department Bulletin for full text of letter.

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BUMED CIRCULAR LETTER 49-103

22 August 1949

To: All Ships and Stations

Subj: Procurement of Medical and Dental Books: Instructions Regarding

Refs: (a) BuMed Cir. Ltr. 48-1; AS&SL Jan-Jun 1948, 48-10, p. 153.
 (b) BuMed Cir. Ltr. 48-73 (Enclosure B); AS&SL Jan-Jun 1948, 48-470, p. 166.
 (c) BuMed Cir. Ltr. 48-143 (Rev. Enclosure B); N.D. Bul., 15 Dec 1948, p. 21.

1. Reference (a), BuMed C/L 48-1, is hereby cancelled and superseded by this letter.
2. Effective immediately, elements of the Medical Supply System will discontinue the stocking and issue of professional, technical, and other medical and dental books. Hereafter, such books shall be obtained through local procurement procedures.
3. In order that activities may obtain current editions of these items in a timely manner, it is strongly recommended that procurement be made through the local sundry purchase procedure in each instance wherein this can be accomplished within the limitations imposed by local and departmental instructions.
4. Funds required for procurement of books shall be included in the "activity annual purchase requisitions" by activities which are granted money allotments. Ships and stations which do not have money allotments granted under the appropriation "Medical Department, Navy," may submit individual purchase requisitions (SandA 76 or SandA 44, as appropriate) for essential professional, technical, and other medical or dental books, to this Bureau for approval.
5. Class 10, and books listed therein, will be deleted from the Army-Navy Catalog of Medical Materiel at a later date. Any residuals resultant to this action, including the Army-Navy Catalog of Medical Materiel, will be carried in class 7.

--BuMed. C. A. Swanson

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BUMED CIRCULAR LETTER 49-104

22 August 1949

To: BuMed Management Control Activities, Continental United States Only.

Subj: Staffing Requirements for Administrative Services; Request for Report on.

Refs: (a) CPI&D 49-64 dtd 22 June 1949.
 (b) BuMed CirLtr 49-100, 17 Aug 1949.

This letter states that when presenting budget estimates for fiscal year 1951 to the Bureau of the Budget, the Bureau of Medicine and Surgery is required to submit reports of staffing for certain administrative services

(civilian personnel functions, fiscal activities, property management, etc.). The Office of Industrial Relations, Executive Office of the Secretary, is accumulating data from selected Medical Department activities for the report on civilian personnel functions (reference a). Data for the fiscal activities report will be made available to the Bureau through the fiscal work measurement program which was established by reference (b). Property management data will be obtained from the Naval Medical Material Office, Brooklyn, N. Y., and the Naval Medical Supply Depots. However, in order to prepare a report on "Other Administrative Services," it is necessary to request certain information from field activities on the following:

- (A) Mail and Messenger Services
- (B) Printing and Duplication
- (C) Library Services
- (D) Maintenance of Premises
- (E) Telephone and Other Communications
- (F) Operation of Motor Vehicles
- (G) Central Files and Stenographic Pools
- (H) Public Relations and Publicity Work

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BUMED CIRCULAR LETTER 49-105

24 August 1949

To: All Ships and Stations

Subj: Hospital Corps Training - Modification of Course in Pharmacy Technic

Ref: (a) Catalog of Hospital Corps Schools and Courses

Encl: (A) Copy of Revised Curriculum

This letter which appears in the 31 August Navy Department Bulletin states that (1) the formal course of instruction for enlisted personnel of the Hospital Corps in Pharmacy Technic currently being conducted at the Naval Medical School, National Naval Medical Center, Bethesda, Maryland, has been extended from six (6) months to nine (9) months (36 weeks of 40 hours each), (2) assignments to this instruction will continue to be made on Bureau quota orders as in the past, (3) students will be accepted on a volunteer basis and will be selected in accordance with the criteria enclosed herewith, and (4) students successfully completing this course will be issued Certificates of Graduation and will be designated Pharmacy Technicians.

The course as shown on enclosure (A) is constituted as follows.

Subject	Clock Hours	
	Theoretical	Practical
PHAR 3 Principles of Pharmacy.....	70	0
PHAR 4 Operative and Dispensing Pharmacy	80	550
PHAR 5 Pharmaceutical Mathematics	90	0
PHAR 6 Materia Medica and Toxicology	170	0
PHAR 7 General Chemistry.....	40	160
PHAR 8 Inorganic Pharmaceutical Chemistry.....	40	160
PHAR 9 Organic Pharmaceutical Chemistry.....	80	0
Total hours	570	870
Grand total		1440

The prerequisites are:

Minimal Qualifications

High School Graduate or equivalent.
 Combined GCT plus ARI score of 100.
 Recommended by senior Medical
 Department officer.
 Twenty-four (24) months obligated
 service from beginning of course.

Desirable Qualifications

High School chemistry.
 Pharmacy experience.
 College training.

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BUMED CIRCULAR LETTER 49-106

24 August 1949

To: All Ships and Stations

Subj: Hospital Corps Training - Establishment of Course in Chemistry
Technic

Ref: (a) Catalog of Hospital Corps Schools and Courses

Encl: (A) Copy of Curriculum

This letter which appears in the 31 August Navy Department Bulletin states that (1) a specialization course in Chemistry technic for enlisted personnel of the Hospital Corps has been established at the Naval Medical School, National Naval Medical Center, Bethesda, Maryland, (2) the course of instruction will cover a period of twelve (12) months (48 weeks of 40 hours each), and will follow, insofar as practicable, the curriculum outlined in Enclosure (A), (3) assignments to this instruction will be made on Bureau quota orders, and students will be selected in accordance with the criteria enclosed herewith, and (4) students successfully completing this course will be issued Certificates of Graduation and will be certified Chemistry Technicians.

The course as shown on enclosure (A) is constituted as follows:

<u>Subject</u>	<u>Clock Hours</u>	
	<u>Theoretical</u>	<u>Practical</u>
CHEM 3 General Chemistry.....	100	162
CHEM 4 Chemical Arithmetic	70	0
CHEM 5 Qualitative Analysis	35	105
CHEM 6 Physical Chemistry.....	28	70
CHEM 7 Quantitative Analysis.....	70	350
CHEM 8 Instrumentation	21	90
CHEM 9 Colorimetry.....	0	15
CHEM 10 Biochemical Procedures	0	15
CHEM 11 Organic Chemistry.....	97	202
CHEM 12 Toxicology.....	<u>120</u>	<u>370</u>
Total hours.....	541	1379
Grand total.....		1920

The prerequisites are:

Minimal Qualifications

High School Graduate or equivalent.
Combined GCT plus ARI score of 110.
Thirty (30) months obligated service
from beginning of course.

Desirable Qualifications

College Chemistry (8 or more
sem. hrs.)
College Physics (8 or more sem. hrs.)
College Mathematics (8 or more
sem. hrs.)
Desire to make career in Navy.

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BUMED CIRCULAR LETTER 49-107

24 August 1949

To: Medical Officers in Command, All Naval Hospitals
District Medical Officers
Staff Medical Officers, Fleet and Type Commands

Subj: MMD, Revised Chapter - Statistical Reporting, NAVMED F, Advance
Information Copy

Encl: 1 (HW) Subject Information Copy

1. It is anticipated that the enclosed revision will be made effective on 1 January 1950, following distribution of the revised Manual of the Medical Department. This advance copy is for information only. NAVMED F (revised 1949) will be available through distribution centers later in the year, but should not be used prior to 1 January 1950.

2. In general the revised NAVMED F reporting system provides for a substantial reduction in the number of NAVMED F cards to be submitted. While the amount of saving will vary with different stations, it is estimated that for the Navy as a whole, the new system will require only two thirds as many reports as does the present system. The principal savings are due to the following provisions:

- (a) Separate reports are not required for convalescent leave.
- (b) Separate reports are not required when an undetermined diagnosis is established.
- (c) Separate reports are not required when a patient is transferred.
- (d) The procedure for reporting continued-remaining cases at the end of the year has been modified to eliminate the majority of such reports.

3. It will be noted that the changes in NAVMED F reporting do not affect the requirement for health record entries of the various changes in status while on the sick list.

4. Printed copies of this revision in pamphlet form will be available for general distribution about 1 November 1949, together with sample copies of the revised NAVMED F. At that time detailed instructions for effecting the change from the old to the new system will be issued.

--BuMed. C. A. Swanson

BUMED CIRCULAR LETTER * * * * *

BUMED CIRCULAR LETTER 49-108

26 August 1949

To: All Dental Officers

Subj: Candidates for U. S. Naval Academy and for U. S. Naval School, Academy and College Preparatory: Dental Examination and Treatment of.

Refs: (a) Par. 2152, Manual of Medical Department.
(b) Par. 3114, Manual of Medical Department.

This letter states that because the number of dental officers allowed the U. S. Naval Academy and the U. S. Naval School, Academy and College Preparatory, is insufficient to permit the acceptance of candidates who fail to meet the dental standards required for candidates for appointment as midshipmen, dental examiners shall:

(a) Find civilian candidates for appointment as midshipmen U. S. Naval Academy not to meet the dental requirements until all carious teeth are restored.

(b) Make every effort to assure that carious teeth in servicemen candidates for the U. S. Naval Academy and U. S. Naval School, Academy and College Preparatory, are restored prior to the time they are to be examined for appointment as midshipmen Naval Academy or for U. S. Naval School, Academy and College Preparatory, training. The dental examiner shall either provide the necessary dental treatment for servicemen candidates who are otherwise qualified or arrange appointments for them with the dental officers of the ships or stations to which the servicemen are attached. When a serviceman candidate is attached to an activity where the services of a naval dental officer are not available, dental care should be provided as directed by reference (b).

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BUMED CIRCULAR LETTER 49-109

26 August 1949

To: Senior Medical and Dental Officers

Subj: Review of Standard Forms 88, 89, and 90, for Purpose of Revision, and Request for Suggestions Relative Thereto,Ref: (a) Letter from Executive Office of the President, Bulletin No. 50-1, dated 19 July 1949.
(b) Standard Forms 88, 89, and 90.Encl: (1) Copy of Reference (a).
(2) Proposed tentative revision of Standard Form 88, drafted by BuMed.

This letter (1) contains information concerning the subject and references, and (2) directs addressees to review subject forms and furnish BuMed with comments and suggestions concerning subject forms by 15 September.

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BUMED CIRCULAR LETTER 49-110

30 August 1949

To: Medical Officers in Command, Naval Hospitals and Hospital Ships

Subj: Standard Staff Locator, NAVMED-1286; Requisitioning of.

Ref: (a) BuMed C/L No. 49-43 dtd 15 Apr 1949.

This letter cancels the provision in reference (a) for ordering subject form and states that requisitions for not over a 3 month's supply should be forwarded to the District Publications and Printing Office.

ALNAV 87

25 August 1949

Subj: Transfer to Regular Navy in MC, DC, and NC

AlNav 27-49 is hereby superseded. Having completed the selection of candidates for transfer to the Dental Corps of the regular Navy that portion of the transfer program under Public Law 347 79th Congress is terminated. Transfer program for appointment in Medical and Nurse Corps remains open.

--SecNav

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